











INVESTOR IN PEOPLE

PRIORITY DOCUMENT

SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b) The Patent Office Concept House Cardiff Road Newport South Wales

NP10 8QQ

REC'D 26 JAN 2004

WIPO PCT

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Signed

Dated 13 January 2004

BEST AVAILABLE COPY

Patents Form 1/77

Cats Act 1977 (Rule 16)



02DEC 7531-1 D00056_ P01/7700-0:00-0227910.7

The Patent Office

Cardiff Road Newport South Wales NP9 1RH

Request for grant of a patent
(See the notes on the back of this form, You can happen an
explanatory leaflet from the Patent Office to help you fill in
this form)

1. Your reference P33779GB/TJF

2. Patent application number (The Patent Office will fill in this part)

0227910.7

29 NOV 2002

3. Full name, address and postcode of the or of each applicant (underline all surnames)

Medical Research Council 20 Park Crescent London W1N 4AL

Patents ADP number (If you know it)

5840624001

If the applicant is a corporate body, give the country/state of its incorporation

United Kingdom

4. Title of the invention

Protein Structure and uses thereof

Name of your agent (if you have one)

"Address for service" in the United Kingdom to which all correspondence should be sent (including the postcode)

Kilburn & Strode 20 Red Lion Street London WC1R 4PJ

Patents ADP number (if you know it)

125001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (if you know it) the or each application number

Country

Priority application number (If you know it)

Date of filing (day / month / year)

 If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application

Date of filing (day / month / year)

 Is a statement of inventorship and of right to grant of a patent required in support of this request? (Answer 'Yes' if:

- a) any applicant named in part 3 is not an inventor, or
- b) there is an inventor who is not named as an applicant, or
- c) any named applicant is a corporate body.See note (d))

YES

Patents Form 1/77 Enter the number of sheets for any of following items you are filing with this form. Do not count copies of the same document Continuation sheets of this form Description 96 Claim (s) Abstract Drawing (s) 5+5 10. If you are also filing any of the following, state how many against each item. Priority documents Translations of priority documents Statement of inventorship and right to grant of a patent (Patents Form 7/77) Request for preliminary examination and search (Patents Form 9/77) Request for substantive examination

Any other documents

(please specify)

(Patents Form 10/77)

I/We request the grant of a patent on the basis of this application.

Signature

29.11.2002

12. Name and daytime telephone number of person to contact in the United Kingdom

FORD, Timothy James Tel: 020 7539 4200

Warning

11.

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977, You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

- a) If you need help to fill in this form or you have any questions, please contact the Patent Office on 0645 500505.
- Write your answers in capital letters using black ink or you may type them.
- c) If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.
- d) If you have answered 'Yes' Patents Form 7/77 will need to be filed.
- e) Once you have filled in the form you must remember to sign and date it.
- f) For details of the fee and ways to pay please contact the Patent Office.

Protein Structure and Uses Thereof

The present invention relates to the crystal structure of pRb/E2F₍₄₀₉₋₄₂₆₎ as well as uses of the structure in identifying agents which modulate the binding between pRb and E2F and/or a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, and thus are useful as pharmaceutical agents in the prevention or treatment of proliferative diseases.

The retinoblastoma tumour suppressor protein (pRb) regulates the cell cycle, sponsors differentiation and restrains apoptosis. Dysfunctional pRb is thought to be necessary for the development of most human malignancies.

pRb controls the cell cycle and apoptosis by acting as a negative regulator of transcription. It is now established that the growth-inhibitory effects of pRb are dependent on its regulation of the E2F family of transcription factors whose activity is necessary for the expression of genes involved in the G1 to S transition of the cell cycle and DNA replication. The transcriptional repression exerted by pRb over E2F responsive promoters involves at least three, distinct mechanisms. By binding to the transcriptional activation domain of E2F, pRb prevents it from recruiting components of the transcriptional apparatus and, once tethered to E2F promoters, pRb interacts with, and represses, other nearby transcription factors. Finally, pRb recruits protein factors to E2F promoters, such as histone deacetylases (HDACs) and histone methyltransferases (HMTases) that negatively regulate transcription by altering chromatin structure.

15

20

In addition to regulating entry into S-phase, it is thought that pRb is important in protecting differentiating cells from apoptosis. Certainly in many types of tissue, loss of pRb leads to apoptosis. This and other data has led to a model whereby the anti-apoptotic activity of pRb is mediated by its repression of certain E2F-dependent promoters. Unrepressed E2F is able to drive apoptosis by both p53-dependent and p53-independent mechanisms.

Although inactivation of the pRb pathway is thought to be widely involved in cellular transformation, there are examples of tumours where over-expression of functional pRb appears to be detrimental to successful clinical treatment. For example, adenocarcinoma of the pancreas is the fifth most common cause of cancer-related death in the Western world. It is particularly resistant to currently available forms of chemotherapy and radiation therapy. It is thought that this malignancy is able to evade apoptosis induced by treatment with chemotherapeutic drugs because of over-expression of pRb. It seems plausible that the protective effect of pRb over-expression against apoptosis is mediated by E2F. By blocking transcriptional activation by E2F, over-expression of pRb appears to render pancreatic cancer cells insensitive to chemotherapy.

. 5

10

15

20

25

30

As many of the anti-tumourigenic properties of pRb are mediated by its regulation of the E2F transcription factors, it would be beneficial to have a crystal structure of the pRb-binding fragment of E2F (E2F₍₄₀₉₋₄₂₆₎) in complex with the tumour suppressor protein. Such detailed knowledge of the molecular interactions between E2F and the A/B interface of pRb would enable the development of compounds that bind to pRb and inhibit complex formation. Such a compound, administered in parallel with conventional chemotherapy, would offer a means of enhancing treatment of proliferative diseases such as pancreatic cancer and perhaps related diseases.

Accordingly, the present invention provides the crystal structure of the primary pRb-binding fragment of E2F (E2F₍₄₀₉₋₄₂₆₎) in complex with the tumour suppressor protein pRb. The structure shows how E2F₍₄₀₉₋₄₂₆₎ binds at the interface of the A and B domains of the pocket of pRb making extensive interactions with conserved residues from both.

In order to address the regulation of the E2F transcription factor by pRb, the present inventors have determined the crystal structure of the complex of pRb_{AB} bound to the

minimal binding region of E2F, namely E2F₍₄₀₉₋₄₂₆₎. The structure has important implications for the understanding of pRb/E2F function. The studies have quantified the contribution of the principal interaction made by E2F through residues 409-426 with pRb as well as that of a secondary interaction involving the marked box region of E2F. In both cases these interactions are with the pocket region of the tumour suppressor protein pRb.

The analysis of the crystal structure of pRb/E2F₍₄₀₉₋₄₂₆₎ suggests that E2F₍₄₀₉₋₄₂₆₎ acts as a sensor of the structural integrity of the pRb pocket. Accordingly, cells in many tissues should be protected against deleterious mutations in pRb because they will sponsor increased E2F transcriptional activation, and thus apoptosis. It seems particularly intriguing, therefore, that all tumour derived pRb mutants fail to bind to E2F suggesting that an intense selectionary pressure operates in many types of tissue in favour of cells which harbour defects in apoptosis once they have lost normal pRb function. Perhaps the most notable exception to this process occurs in retinal cells, which are able to survive for some time with loss of pRb without acquiring other genetic alterations. Indeed, it has been suggested that these particular cells are distinguished by their ability to acquire survival signals from neighbouring cells and thus give rise to the eponymous retinoblastomas.

20

5

10

15

According to a first aspect, the present invention provides a crystal structure of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex, characterised by the atomic co-ordinates of Annex 1.

Preferably the interactions between E2F₍₄₀₉₋₄₂₆₎ and pRb comprise one or more of the following interactions:

E2F ₍₄₀₉₋₄₂₆₎ residue	pRb residue
Leu ₄₀₉	Lys ₅₄₈
Tyr ₄₁₁	Glu ₅₅₁

E2F ₍₄₀₉₋₄₂₆₎ residue	pRb residue
Тут411	Ile ₅₃₂
Tyr ₄₁₁	. Glu ₅₅₄
His ₄₁₂	Arg ₆₅₆
His ₄₁₂	Lys ₆₅₃
Gly ₄₁₄	Glu ₅₃₃
Gly ₄₁₄	Lys ₆₅₂
Leu ₄₁₅	Leu ₆₄₉
Leu ₄₁₅	Glu ₅₅₃
Leu ₄₁₅	Lys ₅₃₇
Glu ₄₁₇	Lys ₅₃₇
Gly ₄₁₈	Arg ₄₆₇
Glu ₄₁₉	Thr ₆₄₅
Arg ₄₂₂	Glu ₄₆₄
Asp ₄₂₃	Arg ₄₆₇
Leu ₄₂₄	Lys ₅₃₀
Phe ₄₂₅	Phe ₄₈₂ .
Phe ₄₂₅	Lys ₄₇₅

In a second aspect, the present invention provides an assay to identify an agent which modulates the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎, the assay comprising:-

- a) combining together pRb, E2F₍₄₀₉₋₄₂₆₎ and an agent, under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ form a complex;
 - b) obtaining a crystal structure of any pRb/E2F(409-426) complex; and
 - c) analysing the crystal structure to determine whether the agent is an agent which modulates the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎.

In the present invention, the term "modulates" is intended to refer to inhibiting, enhancing, destabilising and/or stabilising the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎ and/or the formation of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex and/or the stability of the complex after formation.

5

"conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex" are those conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ form a complex in the absence of an agent. Therefore the effect of the agent on the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎ and complex formation can be assessed.

10

15

30

In the assay, the combining of the pRb, $E2F_{(409-426)}$ and agent may be in any order. The order may be combining pRb with the agent and then adding the $E2F_{(409-426)}$. Alternatively, the order may be combining $E2F_{(409-426)}$ with the agent and then adding pRb, or combining pRb with $E2F_{(409-426)}$ and then the agent. For example, the pRb may be combined with $E2F_{(409-426)}$ before soaking the complex in the agent, preferably in a solution of the agent. In this regard, two of the pRb, $E2F_{(409-426)}$ and agent may be co-crystalised before adding the pRb, $E2F_{(409-426)}$ or agent, as appropriate.

In a third aspect, the present invention provides a method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising selecting an agent using the three-dimensional atomic coordinates of Annex 1.

Preferably, said selection is performed in conjunction with computer modeling.

25 Preferably the method comprises the further steps of:

- a) contacting the selected agent with pRb and E2F₍₄₀₉₋₄₂₆₎ under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex; and
- b) measuring the binding affinity of pRb to E2F₍₄₀₉₋₄₂₆₎ in the presence of the agent and comparing the binding affinity to that of pRb to E2F₍₄₀₉₋₄₂₆₎ when in the absence of the agent, wherein an agent modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex

when there is a change in the binding affinity of pRb to E2F₍₄₀₉₋₄₂₆₎ when in the presence of the agent.

The method may further comprise:

- a) growing a supplementary crystal from a solution containing pRb and E2F₍₄₀₉₋₄₂₆₎ and the selected agent where said agent changes the binding affinity of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex;
 - b) determining the three-dimensional atomic coordinates of the supplementary crystal by X-ray diffraction using molecular replacement analysis;
 - c) selecting a second generation agent using the three-dimensional atomic coordinates determined for the supplementary crystal.

Preferably, said selection is performed in conjunction with computer modeling.

In a fourth aspect there is provided a method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:

- a) contacting a selected agent with pRb and E2F₍₄₀₉₋₄₂₆₎ under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex; and
- b) measuring the binding affinity of pRb to E2F₍₄₀₉₋₄₂₆₎ in the presence of the agent and comparing the binding affinity to that of pRb to E2F₍₄₀₉₋₄₂₆₎ when in the absence of the agent, wherein an agent modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex when there is a change in the binding affinity of pRb to E2F₍₄₀₉₋₄₂₆₎ when in the presence of the agent.

There is a "change in the binding affinity" when the binding affinity either decreases or increases when in the presence of the agent. If a decrease is observed, the agent may be inhibiting the complex. If an increase is observed, the agent may be enhancing the complex.

30

25

10

The method of the fourth aspect may further comprise:

- a) growing a supplementary crystal from a solution containing pRb and E2F₍₄₀₉₋₄₂₆₎ and the selected agent where said agent changes the binding affinity of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex;
- b) determining the three-dimensional atomic coordinates of the supplementary crystal by X-ray diffraction using molecular replacement analysis;
- c) selecting a second generation agent using the three-dimensional atomic coordinates determined for the supplementary crystal

Preferably, said selection is performed in conjunction with computer modeling.

In a fifth aspect, the present invention provides a method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:

15 a) selecting an agent;

5

10

- b) co-crystalising pRb with the agent:
- c) determining the three dimensional coordinates of the pRb-agent association by X-ray diffraction using molecular replacement analysis; and
- d) comparing the three dimensional coordinates with those of the complex as
 claimed in claim 1.

In a sixth aspect, the present invention provides a method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:

- a) selecting an agent;
- b) crystalising pRb and soaking the agent into the crystal;
 - c) determining the three dimensional coordinates of the pRb-agent association by X-ray diffraction using molecular replacement analysis; and
 - d) comparing the three dimensional coordinates with those of the complex as claimed in claim 1.

In a seventh aspect, the present invention provides a method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:

- a) selecting an agent;
- b) co-crystalising pRb, E2F₍₄₀₉₋₄₂₆₎ and the agent;
- 5 c) determining the three dimensional coordinates of the pRb-E2F-agent association by X-ray diffraction using molecular replacement analysis; and
 - d) comparing the three dimensional coordinates with those of the complex as claimed in claim 1.
- In an eighth aspect, the present invention provides a method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:
 - a) selecting an agent;

- b) co-crystalising pRb and E2F₍₄₀₉₋₄₂₆₎ and soaking the agent into the crystal;
- c) determining the three dimensional coordinates of the pRb-E2F-agent association by X-ray diffraction using molecular replacement analysis; and
- d) comparing the three dimensional coordinates with those of the complex as claimed in claim 1.
- Preferably the method of the fifth, sixth, seventh or eighth aspect further comprises selecting a second generation agent using the three dimensional atomic coordinates determined. The agent is preferably selected using the three dimensional atomic coordinates of Annex 1. The selection may be performed in conjunction with computer modeling.
- Preferably the selected agent and/or the second generation agent, in the second, third, fourth, fifth, sixth, seventh and/or eighth aspects mimics a structural feature of $E2F_{(409-426)}$ when said $E2F_{(409-426)}$ is bound to pRb.
- Preferably soaking refers to the pRb/E2F₍₄₀₉₋₄₂₆₎ complex being transferred to a solution containing the selected agent.

The method as defined in the third aspect preferably comprises the further steps of:

- a) contacting the selected agent with the pRb/E2F₍₄₀₉₋₄₂₆₎ complex; and
- b) determining whether the agent affects the stability of the complex.

Preferably the determination is with fluorescence polarization.

In a ninth aspect, the present invention provides a method of identifying an agent that

modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:

- a) contacting a fluorescently tagged E2F₍₄₀₉₋₄₂₆₎ peptide (E2F-fluoroperptide) with pRb to allow pRb/E2F-fluoropeptide complex formation;
- b) detecting the fluorescence polarization;
- c) adding a selected agent; and
- d) detecting the fluorescence polarization in the presence of the agent.

Preferably an increase in fluorescence polarization in the presence of the agent indicates that the agent destabilises the complex.

The method may comprise the further step of adding untagged E2F₍₄₀₉₋₄₂₆₎ and detecting fluorescence polarization.

Preferably if fluorescence polarization decreases, on addition of the untagged $E2F_{(409-426)}$, the agent does not stabilise the complex.

Preferably if there is no substantial change in fluorescence polarization, on addition of the untagged $E2F_{(409-426)}$, the agent stabilises the complex.

The binding affinities may be measured by isothermal titration calorimetry.

Alternatively the binding affinities may be measured by Surface Plasmon Resonance (SPR).

In a tenth aspect, the present invention provides an agent identified by a method according to the second, third, fourth, fifth, sixth, seventh, eighth and/or ninth aspects of the invention.

In an eleventh aspect, the present invention provides an agent, as set out according to the tenth aspect of the invention, for use as an apoptosis promoting factor in the prevention or treatment of proliferative diseases.

Preferably the, or each selected agent is obtained from commercial sources or is synthesised.

Preferably the agent is for use in preventing or treating cancer, which may be pancreatic cancer and related diseases.

15

30

In a twelfth aspect, the present invention provides the use of an agent, which

modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, identified by a method according to the second, third, fourth, fifth, sixth, seventh, eighth and/or ninth aspects of the present invention, in the manufacture of a medicament for the prevention or treatment of proliferative diseases.

The proliferative diseases may be cancer, preferably pancreatic cancer and related diseases.

In a thirteenth aspect, the present invention provides the use of the atomic co-ordinates of the crystal structure as set out according to the first aspect of the present invention, for identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex.

In a fourteenth aspect, the present invention provides computer readable media comprising a data storage material encoded with computer readable data, wherein said computer readable data comprises a set of atomic co-ordinates of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex according to Annex 1 recorded thereon.

The present invention will now be described, by way of example only, and with reference to the following figures, in which:

Annex I.

5

10

Atomic co-ordinates for crystal of pRb/E2F₍₄₀₉₋₄₂₆₎ complex. In Annex 1 there is shown:

Column Number	Description
2 .	Atom number
3	Atom type
4	Residue type
5	pRb domains (A or B) or E2F ₍₄₀₉₋₄₂₆₎ (P)
	·
6	Residue number
7	x co-ordinate of atom (Å)
8	y co-ordinate of atom (Å)
9	z co-ordinate of atom (Å)
10	Occupancy
11	B-factor (Å ²)

Figure 1.

Structure of pRb/E2F.

(A) Schematic drawing of functional domains and protein constructs used for pRb, E2F. The shading used for the constructs in this panel match those used in subsequent figures.

5

- (B) The structure of pRb_{AB}/E2F₍₄₀₉₋₄₂₆₎, shown in two orthogonal views in Ribbons representation. The helices of the A domain are shown as a darker shade to those of the B domain. The main-chain trace of E2F is labelled.
- (C) The interactions between E2F₍₄₀₉₋₄₂₆₎ and pRb_{AB} are shown schematically with the E2F peptide running down the centre. Residues of E2F that are conserved across the five family members are shown as ovals, while the five residue subset of these conserved residues whose mutation leads to disruption of the pRb/E2F interaction are shaded. Hydrogen-bond interactions are shown as broken lines, while hydrophobic contacts are indicated by bands. Residues from domain A of pRb are labelled with an asterisk and the other residues are from domain B. All of the pRb residues shown are either invariant or conserved across 27 species of pRb, p107 and p130.

Figure 2.

20 Isothermal Titration Calorimetry (ITC) measurements.

(A) The upper panel shows the raw data of an ITC experiment performed at 22°C. The lower panel shows the integrated heat changes, corrected for the heat of dilution, and the fitted curve based on a single site model. The panel represents the experiment where E2F₍₂₄₃₋₄₃₇₎ is titrated into Rb_{AB}.

25

(B) Summary of dissociation constants obtained by ITC measurements. The quoted errors are those produced by fitting the data to a two-state model. For the interaction of E2F₍₂₄₃₋₄₃₇₎ to Rb_{AB} and Rb_{ABC} the affinities are too high to measure reliably and we have therefore quoted the upper limits of the dissociation constants.

Structure determination of pRb/E2F

For crystallisation we used a pRb construct based on that previously described by Lee, J.O., Russo, A.A., and Pavletich, N.P. (1998). Structure of the retinoblastoma tumour-suppressor pocket domain bound to a peptide from HPV E7. Nature 391. 859-65, which has engineered thrombin cleavage sites at the ends of the flexible linker region between the A and B domains. Purification and proteolysis produces a final protein containing residues 372 to 589 of the A domain and 636 to 787 of the B domain (hereafter pRbAB - Figure 1A). Although these two domains are not covalently attached after thrombin treatment, they remain tightly associated. The removal of the A-B linker region facilitates crystallisation of pRb but does not alter its 10 binding affinity for E2F. Crystals of the pRb/E2F(409-426) complex grew in a plate-like habit with typical dimensions 200 x 200 x 10 µm³. Repeated attempts at data collection from flash-cooled crystals using synchrotron X-ray sources were thwarted by very high crystal mosaicity and poor data reduction statistics. The problem was 15 overcome by using the micro-focus diffractometer on station ID13 at ESRF current experience and plans at EMBL and ESRF/ID13, Acta Crystallogr D 55, 1765-1770), currently the only such device installed at a synchrotron source. Using a 10x10 um² aperture, data were collected from four separate and widely spaced volumes of a single crystal in order to minimise radiation damage. A total of 100, 1° oscillation images were collected using a MAR CCD detector. These data extended to a Bragg spacing 20 of 2.5 Å with an overall $R_{\text{merge}} = 9.2\%$, and completeness of 87%. The structure was solved by molecular replacement and produced initial electron density maps in which the E2F peptide (E2F₍₄₀₉₋₄₂₆₎) could be readily located.

25 Protein constructs.

Rb_{AB} was expressed as a GST-fusion protein in *E. coli* using the pGEX-6P vector. The construct was engineered to contain a Prescission protease site at the N-terminus of Rb as well as two thrombin sites (LVPRGS) inserted at either end of the flexible A-B linker. Fusion protein was loaded onto a glutathione Sepharose 4B column

before treatment with thrombin and Prescission protease. The resulting eluent was further purified using a Superdex 200 gel filtration column. Rb_{ABC} was expressed in *E. coli* with a C-terminal His-tag using pET-24. Crude lysate was first purified using an S-sepharose column followed by a Ni-NTA step before being run on a Superdex 200 gel filtration column. Recombinant human E2F1₍₂₄₃₋₄₃₇₎ was expressed in *E. coli* using pGEX-6P with an engineered Prescission protease site at the N-terminus of E2F. Crude lysate was bound onto a glutathione Sepharose 4B column prior to cleavage with the protease. The resulting eluent was further purified by gel filtration on a Superdex 75 column. E2F₍₄₀₉₋₄₂₆₎ and E2F₍₃₈₀₋₄₃₇₎ were synthetic peptides. HPV-16 E7₍₁₇₋₉₈₎ was prepared as described elsewhere (Clements, A.J., K, Mazzareli, J.M. Ricciardi, R.P. Marmorstein R. (2000). Oligomerization properties of the viral oncoproteins adenovirus E1A and human papillomavirus E7 and their complexes with the retinoblastoma protein., Biochemistry 39, 16033-16045).

15 Crystallography.

Plate-like crystals were grown by the hanging drop vapour diffusion method at 4°C.

Rb_{AB} was mixed with the E2F-1 peptide at 1:2 molar ratio and concentrated to

15mg/ml. Hanging drops were formed by mixing 1µl of protein solution with an equal volume of reservoir solution containing; 0.14M Na citrate, 26% PEG400, 4%

n-propanol and 0.1M Tris at pH 7.8. Crystals were flash frozen in mother-liquor made up to 25% glycerol. Diffraction data were collected using the micro-focus diffractometer at ESRF and processed using the DENZO and SCALEPACK software (Otwinowski, Z.M., W. (1993). In Data Collection and Processing, L.I. Sawyer, N. Bailey, S., ed. (SERC Daresbury Laboratory), pp. 556-562). Molecular replacement calculations were carried out using Amore (CCP4, 1994) with 1GUX.brk as the search model. The final model contains co-ordinates for the protein which cover residues 379-578 of the A domain and 644-787 of the B domain of Rb and the entire E2F₍₄₀₉₋₄₂₆₎ peptide for the four copies present in the asymmetric unit together with 600 solvent

molecules. The refined model has the following residuals; $R_{work} = 23.7\%$, $R_{free} = 28.7\%$, rmsd bonds = 0.007 Å, rmsd angles = 1.3°.

Structure of pRb/E2F complex

- The packing of the A and B domains generates a waist-like interface groove into which E2F₍₄₀₉₋₄₂₆₎ binds in a largely extended manner (Figure 1b). The peptide makes contacts with residues from helices $\alpha 4$, $\alpha 5$, $\alpha 6$, $\alpha 8$ and $\alpha 9$ of domain A, and with $\alpha 11$ from domain B of pRb. Formation of the complex buries 2280 Å² of surface area. 1500 Å² of which are hydrophobic. The two end regions of the E2F₍₄₀₉₋₄₂₆₎ fragment make extensive contacts with pRb, while interactions made by the middle section of the E2F₍₄₀₉₋₄₂₆₎ fragment (residues 416 to 420) are relatively sparse (Figure 1C). Overall, a high proportion of the hydrogen bond interactions between the two molecules involves the side chains of conserved pRb residues interacting with the main chain of E2F. Examination of the distribution of conserved residues over the 15 surface of pRb, reveals that the majority are accounted for by the E2F binding site. There is a somewhat smaller cluster of conserved residues associated with the LxCxE binding site. Perhaps the most remarkable aspect of this analysis is that although pRb has been reported to associate with at least 110 cellular proteins perhaps 50 or more in a pocket-dependent manner, the E2F and LxCxE binding sites account for almost all of the conserved residues on its surface. There are two explanations that may partially 20 account for these observations. Firstly, many of the reported binding partners of pRb have yet to be verified. Secondly, the LxCxE binding site is probably responsible for mediating the binding of many different proteins, such as HDAC, to pRb.
- Since there are four copies of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex in the asymmetric unit of our crystal form it is possible both to compare these four crystallographically independent copies of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex and to compare them with the crystal structure of pRb/E7 without bond E2F (Lee et al., 1998 Supra). The first six residues at the N-terminus, the α3-α4 and α6-α7 loops adopt different conformations

5

10

15

20

25

between the four copies in our asymmetric unit, while the variations across the rest of the structure between the four molecules is not significant. Comparison of the pRb structure in the presence and absence of bound E2F(409:426) shows that there is essentially no change in the relative orientation of the two lobes of the A/B pocket on E2F₍₄₀₉₋₄₂₆₎ binding nor any widespread changes in the structures of the individual domains. This comparison does reveal that the end of 0.4 and the connecting loop to α 5 becomes ordered in the pRb/E2F₍₄₀₉₋₄₂₆₎ complex as two conserved residues (Glu464-pRb & Arg467-pRb located towards the end of α4 in our structure) interact with the E2F₍₄₀₉₋₄₂₆₎ peptide. Within the E2F₍₄₀₉₋₄₂₆₎ construct there are eight residues that are conserved across E2F's from all animal species (Figure 1A). Amino-acid substitutions at five of these positions have been shown to lead to loss of binding to pRb but retention of E2F's trans-activation potential. The following description focuses on the structural role of these five residues. Tyr(411)-E2F appears to play an important role in peptide binding because its phenolic ring occupies a hydrophobic pocket created by Ile(536)-pRb, Ile(532)-pRb, Ile(547)-pRb and Phe(413)-E2F, while its hydroxyl group makes a hydrogen bond to the invariant Glu(554)-pRb. Towards the C-terminal part of the E2F peptide, Leu(424)-E2F and Phe(425)-E2F make several hydrophobic interactions, two of which involve conserved residues. Leu(424)-E2F makes contacts with the aliphatic portion of the side chain of Lys(530)-pRb and also packs against Leu(415)-E2F and Phe(425)-E2F. In addition, Phe(425)-E2F itself packs against Phe(482)-pRb. Unlike the residues of E2F just discussed, the side-chains of Glu(419)-E2F and Asp(423)-E2F do not point into the groove formed between the A and B domains of pRb, but instead point away from it. Glu(419)-E2F hydrogen bonds through a water molecule with the main-chain carbonyl of Thr(645)-pRb; Asp(423)-E2F forms a salt bridge with Arg(467)-pRb located at the end $\alpha 4$.

Finally, as described earlier, the crystal structure shows how E2F makes extensive contacts with largely conserved residues from both the A and B domains of the pocket

and that the binding site for E2F is dependent on the structure of the interface between the two domains. This feature of the structure suggests that E2F acts as a sensor of the structural integrity of the pRb pocket. The position and nature of the E2F binding site make the binding of the transcription factor particularly sensitive to mutations in the pocket region of the tumour suppressor protein. The potential significance of these observations will be discussed later with regard to the normal role of pRb in protecting cells against E2F-mediated apoptosis.

Additional determinants of pRb/E2F function

It is clear from a number of studies that, although E2F(409-426) expressed as a Gal4 10 fusion protein is sufficient to recruit pRb and repress transcription, there are additional interactions made by the physiologically relevant E2F/DP heterodimer with pRb. Similarly, while the pocket domain is highly conserved, the most frequent site of deleterious mutation, and capable of transcriptional repression, it is not sufficient for 15 the physiological function of pRb. In particular, the C-terminus of pRb is necessary for mediating growth arrest and recruitment of certain cyclin/cdk complexes as well as containing several of the residues whose phosphorylation leads to deactivation of pRb function. Therefore, in order to better understand the requirements for physiological pRb/E2F complex formation, we have made a series of constructs of the two proteins 20 (Figure 1A) and carried out binding measurements by isothermal titration calorimetry (ITC). We have also carried out a series of competition experiments to confirm qualitatively the interpretation of the ITC binding data.

Isothermal Titration Calorimetry.

Binding of the various E2F constructs to Rb_{AB} and Rb_{ABC} was measured by isothermal titration calorimetry using a MicroCal Omega VP-ITC machine (MicroCal Inc., Northampton, USA). The E2F constructs at a concentration between 100-150 μM were titrated into 12-15 μM Rb at a temperature of 22°C. Proteins were dialysed against 50mM Tris pH 7.6, 100mM NaCl and 1mM TCEP. After subtraction of the

dilution heats, calorimetric data was analysed using the evaluation software MicroCal Origin v5.0 (MicroCal Software Inc.). For all of the titrations, the stoichiometry of ligand binding to Rb was very close to 1.0. For E2F₍₂₄₃₋₄₃₇₎ binding to Rb, the binding affinity and the heat change associated with binding were such that we could only establish that binding was tighter than 10 nM. In order to verify that binding of this protein was similar for both Rb_{AB} and Rb_{ABC} we carried out competition experiments which showed approximately equal partition between the two different Rb proteins.

Competition experiments.

5

10 The proteins used in these experiments were His₆-Rb_{ABC} (RESIDUES 380-929); MW 66.07kDa, non-tagged Rb_{AB} (residues 372-787); MW 48.67 KDa, are His₆-Rb_{AB} (residues 376-792); MW 49.86 KDa, E2F₍₂₄₃₋₄₃₇₎; MW 21.45 KDa HPV E7 (residues 17-98); MW 9.38 KDa and E2F₍₄₀₉₋₄₂₆₎; MW 2.12 KDa. Protein concentrations were carefully determined by u.v. spectroscopy and confirmed by ITC titrations. The small 15 acidic E2F proteins stain much weaker than Rb with Coomassie on SDS-PAGE. For all gel lanes contained a final RbAB concentration of ca. 7 µM. After equilibration with E2F₍₂₄₃₋₄₃₇₎ and E2F₍₄₀₉₋₄₂₆₎ the samples were loaded onto a 1.0ml Ni column and washed with 7 x 0.5 ml of loading buffer (50mM Tris pH 7.5, 200mM NaCl & 10mM Imidazole). The samples were then eluted with 7 x 0.5ml elution buffer (50mM Tris, 20 pH 7.5, 200mM NaCl, 200mM Imidazole). After volume correction samples were boiled in SDS loading buffer and run on a 4-12% SDS PAGE. For the two pRb proteins and E2F₍₂₄₃₋₄₃₇₎ were mixed at 40µM in a final volume of 0.5ml. After equilibration for 2hrs the mixture was loaded onto 1ml Ni beads in a small column, washed with 7 x 0.5ml of loading buffer (50mM Tris, pH 7.5, 200mM NaCl, 10mM 25 Imidazole), eluted using 7 x 0.5ml elution buffer (50mM Tris, pH 7.5, 200mM NaCl, 200mM Imidazole). Samples, after correcting for volume were boiled in SDS sample buffer and run on a 4-12% SDS gel.

A typical ITC experiment is shown in Figure 2A and a summary of the affinity constants obtained for both pRbAB and pRbABC interacting with three constructs of E2F are given in Figure 2B. The two shorter E2F constructs bind to either pRbAB or pRb_{ABC} with similar affinities. However, E2F₍₂₄₃₋₄₃₇₎ binds at least 16-fold stronger than either of the two shorter E2F fragments to both pRbAB and RbABC. Our ITC data therefore show that there are additional interactions of the A/B pocket of pRb with a region of E2F-1 outside of the transactivation domain. This result has been confirmed qualitatively by competition experiments which show that a 15-to 30-fold molar excess of the shorter E2F peptide is required to 50% compete with E2F₍₂₄₃₋₄₃₇₎ for binding to pRb. Our results are consistent with an earlier report that noted an interaction of pRb with the marked box region of E2F (residues 245-317). Taken together, these data demonstrate that the majority of the free energy of interaction between pRb and E2F is contributed by the 18-residue segment E2F₍₄₀₉₋₄₂₆₎ used in our structure analysis. There is an additional stabilising interaction between the marked box region of E2F and pRb, that contributes approximately 2kcal mol⁻¹ to the overall free energy of complex formation, but is not sufficient on its own for complex formation.

10

15

20

As the binding constant for the interaction of E2F₍₂₄₃₋₄₃₇₎ with pRb_{AB} (or pRb_{ABC}) was too tight to determine reliably by ITC we performed a competition experiment to determine if this E2F construct bound preferentially to one or the other pRb construct. The results show approximately equal partitioning of E2F₍₂₄₃₋₄₃₇₎ between the two pRb species and demonstrates therefore, that the C-terminus of pRb does not participate in the binding to E2F-1 in isolation. This means that in addition to the interaction of E2F₍₄₀₉₋₄₂₆₎ with the pocket region of pRb there is an additional interaction, almost certainly involving the marked box region of E2F, that also binds to the pRb pocket. This data is consistent with the hypothesis that the approximately 10-fold stronger interaction of E2F/DP with pRb_{ABC} rather than pRb_{AB} reported previously arises through interactions of the DP component of the E2F/DP heterodimer with the C-terminus of pRb. This ideas is strongly supported by the data from another study 30

which shows that DP-1 interacts with pRb in a manner that does not require the structural integrity of the A/B pocket. Taken together, these data indicate that at least one of the functions of the C-terminus of pRb is to bring additional stabilisation to the interaction of the tumour suppressor with the heterodimeric E2F/DP transcription factors.

Use of structure atomic co-ordinates of Annex I

The atomic co-ordinates of Annex 1 are cartesian co-ordinates derived from the results obtained on diffraction of a monochromatic beam of X-rays by the atoms of the pRb/ $E2F_{(409-26)}$ complex in crystal form. The diffraction data was used to calculate electron density maps of the crystal. The electron density maps were then used to position the individual atoms of the pRb/ $E2F_{(409-26)}$ complex.

The determination of the three-dimensional structure of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex provides basis for the design of new and specific agents that modulates formation of the complex and/or modulates the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎. For example, computer modelling programs may be used to design different molecules expected to modulate formation of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex and/or the interactions between pRb and E2F₍₄₀₉₋₄₂₆₎.

20

15

5

10

A candidate agent, may be any available compound. A commercial library of compound structures such as the Cambridge Structural Database would enable computer based *in silico* screening of the databases to enable compounds that may interact with, and/or modulate formation of, the complex to be identified.

25

Such libraries may be used to allow computer-based high throughput screening of many compounds in order to identify and select those agents with potential to modulate formation of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex and/or the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎.

In this regard, a potential modulating agent can be subjected to computer modelling with a docking program such as GRAM, DOCK or AUTODOCK (see Walters et al., Drug discovery Today, Vol.3, No. 4, (1998), 160-178, and Dunbrack et al., Folding and Design, 2 (1997) 27-42) to identify and select potential agents. This can include computer fitting of potential modulating agents to the pRb/E2F₍₄₀₉₋₄₂₆₎ complex to ascertain how the agent, in terms of shape and structure, will bind to the complex.

Computer programs can be employed to estimate the interactions between the pRb, E2F₍₄₀₉₋₄₂₆₎ and agent or pRb/E2F₍₄₀₉₋₄₂₆₎ complex and agent. These interactions may be attraction, repulsion, and steric hindrance of the two binding partners (e.g. the pRb/E2F₍₄₀₉₋₄₂₆₎ complex and a selected agent). A potential agent will be expected to be more potent if there is a tighter fit and fewer steric hindrances, and therefore greater attractive forces. It is advantageous for the agent to be specific to reduce interaction with other proteins. This could reduce the occurrence of side-effects due to additional interactions with other proteins.

Potential agents that have been designed or selected possible agents can then be screened for activity as set out in the second to seventh aspects above. The agents can be obtained from commercial sources or synthesised. The agent is then contacted with pRb/E2F₍₄₀₉₋₄₂₆₎ complex to determine the ability of the potential agent to modulate the formation of the complex. Alternatively the agent may be contacted with pRb and E2F₍₄₀₉₋₄₂₆₎ under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex (in the absence of agent), to determine the ability of the agent to modulate complex formation.

25

5

10

15

- 20

A complex of pRb/E2F₍₄₀₉₋₄₂₆₎ and said potential agent can then be formed such that the complex can be analysed by X-ray crystallography to determine the ability of the agent to modulate complex formation and/or the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎.

The complex of pRb/E2F₍₄₀₉₋₄₂₆₎ and agent could be compared to that for pRb/E2F₍₄₀₉₋₄₂₆₎ alone.

Detailed structural information can then be obtained about the binding of the potential agent to the complex. This will enable the structure or functionality of the potential agent to be altered to thereby to improve binding. The above steps may be repeated as may be required.

The agent-pRb/E2F₍₄₀₉₋₄₂₆₎ complex could be analysed by:

25

co-crystallising pRb/E2F₍₄₀₉₋₄₂₆₎ with the selected agent or soaking the agent into crystals of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex; and then determining the three dimensional co-ordinates of the agent-complex by X-ray diffraction using molecular replacement analysis.

Therefore, the pRb/E2F₍₄₀₉₋₄₂₆₎ -agent complexes can be crystallised and analysed using X-ray diffraction data obtained and processed, for example using the DENZO and SCALEPACK software (Otwinowksi, Z. M., W. (1993).Difference Fourier electron density maps can be calculated based on X-ray diffraction patterns of soaked or co-crystallised pRb/E2F₍₄₀₉₋₄₂₆₎ complex and the solved structure of uncomplexed agent. These maps can then be used to determine the structure of the agent bound to the pRb/E2F₍₄₀₉₋₄₂₆₎ and/or changes in the conformation of pRb/E2F₍₄₀₉₋₄₂₆₎ complex relative to the pRb/E2F₍₄₀₉₋₄₂₆₎ complex in the absence of agent.

The agent may be improved, for example by adding or removing functional groups, substituting groups or altering its shape in light of data obtained from agent bound to pRb/E2F₍₄₀₉₋₄₂₆₎ complex and/or agent bound to pRb. Such an improved agent may then be subjected to the methods of the invention.

Electron density maps can be calculated using programs such Amore from the CCP4 computing package (Collaborative Computational Project 4. The CCP4 Suite:

Programs for Protein Crystallography, Acta Crystallographical, D50, (1994), 760-763).

The provision of computer readable media enables the atomic co-ordinates to be accessed to model the pRb/E2F₍₄₀₉₋₄₂₆₎ complex by, for example, RAMSOL (a publicly available computer software package which allows access and analysis of atomic co-ordinate data for structure determination and/or rational drug design).

In addition, structure factor data, derivable from the atomic co-ordinate data (see e.g. Blundell et al., in Protein Crystallography, Academic Press, New York, London and San Francisco, (1976)), can be used to enable difference Fourier electron density maps to be deduced.

Screening assays

5

20

After an agent has been selected, its inhibitory effect on pRb/E2F₍₄₀₉₋₄₂₆₎ complex formation or ability to interact with the pRb/E2F₍₄₀₉₋₄₂₆₎ complex can be assessed with one or more of the assays of the invention.

For example, the crystal structure of the interaction of $E2F_{(409-426)}$ with pRb can be used to aid the design of a fluorescently tagged peptide for the use in a binding assay suitable for high throughput screening of low molecular weight compounds or peptide libraries. The fluorescent tag may be a fluorescein, rhodamine or some other commercially available tag chemically attached via a suitable amine or thiol group.

Binding could be measured by detecting fluorescence polarization in an homogeneous assay format (i.e. one in which all reagents are mixed in a single well, and reaction occurs in solution without wash steps). Fluorescence polarization technology is commonly applied in high throughput screening laboratories (ref: Sokham et al. (1999) Analytical Biochemistry, 275, 156-161. "Analysis of protein-peptide interaction by a

miniaturised fluorescence polarization assay using cyclin-dependent kinase2/cyclin E as a model system.")

Fluorescence polarization can be used to determine binding of a fluorescently- tagged small molecule (ligand or peptide) with a large molecule (receptor or protein) by detecting changes in the rotational velocity of the small molecule in the free and bound state. The rotational velocity is inversely proportional to the size of the molecule.

Using suitable optics these changes in rotational velocity can be measured as a differences in light transmitted in parallel and perpendicular to a polarized excitation source.

In the assay of the present invention, fluoro-peptide (E2F₍₄₀₉₋₄₂₆₎—fluoropeptide) bound to pRb will have a low rotational velocity and will appear stationary during the excitation period. Emitted light will be transmitted in parallel to the polarized incident light and the light detected will have a high polarization value. In contrast in the presence of an inhibitor of the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎—fluoropeptide, the free E2F₍₄₀₉₋₄₂₆₎—fluoro-peptide will have a high rotational velocity and light will be transmitted in all directions. Emitted light will be detected both parallel and perpendicular to the polarized excitation source, and will have a low polarization value. If the rotational velocity does not increase in the presence of the agent but, on addition of E2F₍₄₀₉₋₄₂₆₎ which is not fluorescently tagged, the rotational velocity does increase, this leads to the agent destabilising the complex. Alternatively if the rotational velocity does not increase, this leads to the agent stabilising the complex.

25 In this regard an assay could include the following steps:

15

- 1. Allow complex formation of pRb/E2F₍₄₀₉₋₄₂₆₎-fluoropeptide and measure max fluorescence polarization (FP);
- 2. Add agent no change in FP, no disruption of complex;
- 3. Add unlabeled E2F expect displacement of E2F₍₄₀₉₋₄₂₆₎-fluoropeptide and a
 decrease in FP, but not if complex is stabilised by presence of reagent.

The Interactions could be confirmed by co-crystalisation of pRb/E2F₍₄₀₉₋₄₂₆₎ with agent, and determination of the three dimensional atomic coordinates by X-ray diffraction and molecular replacement.

5

10

The E2F₍₄₀₉₋₄₂₆₎/pRb interaction can also be applied to heterogeneous assay formats (i.e. ones in which reagents are partitioned between a solid support and in solution, and wash steps are involved). This would involve the immobilisation of pRb on microtitre plates, for example by antibody capture or metal ion chelation using Histagged pRb and Nickel coated plates. E2F₍₄₀₉₋₄₂₆₎ peptide may be tagged with fluorescence as above and the fluorescent detected directly to determine amount bound. Alternatively, the peptide could be labelled with biotin and detected with streptavidin-horse radish peroxidase in an ELISA-like format.

15 Compounds which interact with the complex without altering association or disassociation of the complex could be identified by crystallographic means, unless the agent itself was tagged (radioactivity/fluorescence) and binding to the complex measured directly, eg fluorescence polarization as above or scintallation counting of

. 20

25

an immuno-precipitate.

Alternatively, the agent can be added to pRb and $E2F_{(409-26)}$ under conditions in which pRb and $E2F_{(409-26)}$ can form a complex. This could result in the agent and complex cocrystallising. The binding affinities of pRb to $E2F_{(409-26)}$ in the pRb/ $E2F_{(409-26)}$ complex in the presence and absence of the agent can then be compared to determine whether the agent inhibits complex formation. The three dimensional structure of the pRb/ $E2F_{(409-26)}$ – agent complex can also be solved to enable the associations in the new complex to be compared with those in the pRb/ $E2F_{(409-26)}$ complex (see Annex 1).

As a further alternative the pRb/ $E2F_{(409-26)}$ complex can be formed before soaking the complex in the presence of a selected agent. The binding affinities of pRb to $E2F_{(409-26)}$ can then be determined in the presence and absence of the agent. As before, the three dimensional structure of any pRb/ $E2F_{(409-26)}$ – agent complex could be solved.

5

The binding affinities can be measure using isothermal titration calorimetry.

Alternatively, surface plasmon resonance could be used such as that provided by Biacore.AB.

Preferred features of each aspect of the invention are as for each of the other aspects mutatis mutandis. The prior art documents mentioned herein are incorporated to the fullest extent permitted by law.

	2 2	×	ن	ပ	ပ	က ်	υ i	υ d) ;	Z (O (י כ	ວ່ ເ	> ;	Z, (ပ (0 :	Z (ပေး	ပ (0 (י כ	ن ن	o :	Z ·	u ا	ပ (บ	ပ	ບ	ပ	0	z	ပ	ບ	ບ	ບ
asymmetric	gama=90.00						٠. ق									•																					
in an	heta=93.70 gam	45.1	.00 44	1.00 44.57	1.00 45.87	'n	52.37	0.43.3	43.6	41.4	39.8	30.00	40	40.	36.	38.6	ო დ	36.8	35.5		ന	35.3	33.3	32.	31.	0 30.2	0 30.	0 29.0	0 33.0	0 28.3	0 29.8	30.5	0 29.5	0 29.7	0 29.9	m 0	1.00 39.96
r molecules	00	30.44	9.0	2.02	3.13	34.740	35.114	0.44	0.82	9:90	9.64	9.70	1.13	31.937	.46	.27	7.35	8.12	6.81	. 80	. 79	. 24	.28	27.043	24.971	. 26	22.782	21.938	•	22.531	24.767	•	•	Ŋ	. 82	Ġ	26.137
from four	ט = בילה [מ הפלה [מ	-15,752	-16.486	08	90	•	-17.831	-15.543	-15,889	-14.348	-13.347	93	.44	44.	i	-13.550	-14.006	. 19	3.25	.21	•	•	1.90	.02	-11.770	ö	•	. 609 * 6-	-8.721	નં	-10.020	-8.833	-10.942	-10.639	. 94	. 70	-12.955
one molecule	crystal:		•	•	90.	•	10.805	10.802	9.681	11.069	10.043	10.641	10.867	. 92	12.115	9.449	10.144	•	•	•	•	•	7.123	•	7.170	. 6.820	•	•	7.902	•	5.498	. 5.258	4.638	3.305	2.535	1.103	0.261
 13	In the	158.548 226 k	ζ,		4	(4	A 37	A 37	A 37	ASN A 380	ASN A 380	ASN A 380	ASN A 380	đ	THR A 381			THR A 381	THR A 381	THR A 381	ILE A 382	ILE A 382	ILE A 382		ILE A 382			ILE A 382	GLN A 383	GLN A 383	GLN A 383		GLN A 383				
	д,	9	2 f	_					0	N	4	G G	CG 7		ND2 P				_	CB J		CG2 1	ບ	0	N	ر ا	C B				ט	0	Z	g g	8	_	8
the co		a=101	⊣ (7 (J 4	ት ሲ	ω	7	ω	σ	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
REMARK		XX	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM .	ATOM	ATOM	ATOM	ATOM	ATOM

0 2	3 (ပ ()	Z (ນ ເ	ບ	U (บ	0	Z	ပ	0	Z	บ	บ	υ	ບ	U	บ	0	Z	ບ	ט	O	യ	ບ	ບ	0	z	ບ	บ	ပ	ຜ່	U	ပ	0	Z	บ	.	ບ	ე,
		0 27.9	.00 27.2	0 26.5	0 24.	26.4	0 29.9	0 35.6	.00 33.7	37.	.00 23.5	0 23.1	.00 21.	19.4	0 20.	0.0	6.8	0 22.	18.6	7.7	1.00 16.78	16.2	0 16.	.00 14.4	.00 20.6	17.3	0 15.4	.00 14.4	14.	15.3	0 16.6	0 21.	0 33.3	9.3	0 13.	'n	1.9	.00 10.0	1.00 11.21	0 10.6	ന
ന	2 / 2	6.79	ė.	7.79	8.97	0.14	0.00	1.18	1.42	•	.77	. 24	.05	•	. 12	•	o,	Ġ	o,	Ξ.		٦.	٥.						27.085		-	03	23	29.834	81	0	27	0	0.5	1.55	2.1
122	4.07	.72	8.90	.86	. 05	•	9.95	0.83	1.97	•	7.61	.67	•	.05	-5.976	•	.61	-4.708	.38	-4.175	•	-5.561	.48	. 11	-7.361	-6.895	-5.117	: 15	-5.823	-5.451	. 63	. 70	. 84	-9.970	•	-3.369	. 18	.09		.61	-5.022
	8	•	2.247	.01	o,	ø.	٦.	6.694	ď	9	4.371		4.	α.	7		•	•	•	4.598		•	•	•	•	•	•	.30	1.641	•	.08	99.	.47	.08	.81	.0	.04	.51	3.933	.83	5.163
A I	A 38	38	GLN A 383	38	GLN A 384	വ	w	A 3	പ	A 3	ø	GLN A 384	LEU A 385		ø	ø		Þ	ø			Ą	ന	A 3	MET A 386	A 3	A 3	MET A 386	MET A 387	ന	A 3	A 3	A 3	MET A 387	S.	m	A 3	A 3	ILE A 388	A 3	
	NE2 G	ບ	0	N G	9 5	CB	D D	მ	· .	NE2 G		0		_														_	N		-	CG M			_	_	N		CB	CG1 I	_
37	38	39	40	41	42	43	44	45	46	47	48	49	20	51															99		68	69	70	7.1	72	73	74	75	92	11	78
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

ບບຸ	0 2	; U	บ	ບ	U	ບ ,	Ü	0	z	Ö,	ပ	ບ	0	Z	ບ	0	Z	ບ	Ö	0	ບ	0	Z	ບ	ບ	ບ	0	N	ບ	ပ	0	ບ	0	Z	ບ	ບ	ָט	o,	0
																			٠,															•					
9.99	H 0		o,	o,	٥.	٥.	۰.	7	۰.	ᅼ.	ų.	ĸ.	۰.	۲.	ᅼ	۰.	۲.	7.59	7.30		7.70	æ	4.	æ	4.	8.43	. 7	4,	11.12	11.04	۲.	٥.	ú	•	11.53	œ	15.82	17.94	18.22
1.00	0		0	0	0	0	0	0	0	0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00.1	1.00	1.00	1.00	1,00	1.00 1	1.00 1	1.00 1
31.211	29.723	2.24	. 근	Ġ	5.08	7.	6.74	ė.	6.48	26.080	. 75	.31	.50	.94	27.084	26.653	28.385	29.338	30.413	31.241	30.005	30.608	29.872	30.415	30.091	29.860	8.75	0.63	•		•	29.385	29.408	ιċ	27.679	26.524	25.569	24.658	25.673
-2.204	ω.	-1.633 -0.600	. 6	σ	-0.770	•	•	•	-1.196	•	•	-2.597	-1.844	-3.753	-0.146	0.694	-0.344	0.461	-0.391	-1.006	1.626	ຜ	•	2.673	2.367	4.043	4.150	5.087	.48	7.253	8.586	7.157	6.842	8.108	8.875	9.445	8.353	7.926	7.835
4.646	1.938	3.028	4.037	5.546	6.365	6.148	1.681	1.326	0.872	-0.485	-1.197	-1.054	-0.467	-1.582	-1.269	-2.038	-1.074	-1.849	-2.517	-1.555	-1.091	-1.696	0.233	1.082	2.494	0.695	0.169	0.958	0.655	0.692	0.415	1.651	2.838	1.167	1.987	1.133	0.624	1.378	-0.509
ILE A 388 ILE A 388	Ø,	LEU A 389 FEIT A 389	€ 4	Ø	ď	ø	LEU A 389	ø	4	ď	ASN A 390	ø	ď	ø	4	Ø	ø	A	SER A 391	ø	ď	ď	ď	ø	ø	ø	ď	ď	4	ď	ø	SER A 393	SER A 393	ASP A 394	A 3	ASP A 394	SP A 394	ASP A 394	ASP A 394
CG2							ر ن																											N				_	OD2 A
79	81	0 00	8 48	85	86	87	88	89	90	91	92	93	94	95	96	97	98	66	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM.	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

-

.

.

	U	0	z	บ	U ·	U	ບ	0	Z	U	0	z	บ	บ	ບ	ບ	ບ	0	Z	ບ	ប	0	ບ	0	n	ט	ပ	ບ	ָט י	0	0 1	บ	0	Z	บ	บ	ט	0	×	O	0	N
·	00.	12.7	.00 10.	.00 10.4	.00 11.8	.00 14.7	.00 17.3	.00 13.5	.00 15.3	.00 8.5	.00 7.5	.00 7.5	.00 8.1	.00 6.7	0.9 00.	6.7	.00 8.6	.00 9.7	.00 8.4	6.6 00.	.00	.00 6.5	.00 10.7	.00 10.	.00 12.2	ທີ	.00 16.0	.00 22	30.6	.00 28.5	0 34.6	.00 14.6	.00 14.3	.00 15.3	1.00 15.54	.00 17.6	ų.	.00 29.1	1.00 26.01	.00 14.4	0	1.00 11.35
	8.3	•	9.	o.3	o. 0.		8.8	7.6	9.3	ä	2.00	. 94	3.10	3.32	2.08	1.37	4.33	.50	5.18	6.31	6.91	7	.39	7.34	.38	9	0.49	.76	σ,	0.01	8	0.17	0.55	0.25	. 82	g	.31	.55	.21	90.	0.5	38.663
	10.030	•	0.7	Η.	2.1	12.872	3.68	3.8	14.156	œ		1.7	1.3	2	ж. Ж.	13.040	0.	1.69	.16	.81	8.437	•	10.829	99.	10.725	11.583	15	0.72	9.4	2.8	.i	다. 작.	2.44	10.286		9	.27	8.543	.74	.67	11.219	.58
	•	3.497	•	•	•	•	•	•	•	•	•	•	5.567	4.	ų.	5.063	4.665	ø.	•	4.221	4.561	5.712	•	•	•	3.529	•	•	0.312	•	.01	•	'n	4.		ο.	πi		•	7.843	8.811	. 74
	39	ø		GLN A 395		GLN A 395			GLN A 395		GLN A 395	Ø	ø	Ø	PRO A 396	ď	PRO A 396	ď		ø		ø	Ø	Ø	ď	GLU A 398	ø	ď	ď	ď	ø	ø	ď	A 3	ന	E A	ന	m	A 3	ď	A 3	4
	<u>ი</u>	0	8	_	_	_			•		0	•														5		უ წ		_			0	•	_		_	OD1	ND2	ບ	0	z
	121	122	123	124	125	126	12.	128	125	130	131	132	133	134	135	136	137	138	135	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162
	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

																														٠											
	•	o.	•			. •	•	۲.	•	Ģ	•	٥.	٥.	•	æ	9.50	0.2	14.32	•	9	9.50	6.67	9.50	10.54	11.31	9.55	10.21	a	•	•	•	•	•	8.77	9.18	6.14	۲.	2.70	2.00	2.00	
	1.00	1.00	0.	•	1.00	•	•	•	•	•	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	٥.	۰.	٥.	٥.	1.00	°	°.	٥.	1.00	1.00	1.00	1.00	1.00
œ	6	5.63	4.10	•	7.9	8.04	8.00	œ.	.15	36.732	5.7	8.66	9.58	•	ö	41.773	•	43.782	41.604	•	40.852	40.585	9.81	•	•	42.276	42.063	•	41.171	.47	39.824	.16	.83	38.133	36.997	35.902	•	34.869	33.889	33.939	4.9
11.137	ö	10.282	.35	1.0	2.67	13.239	w.	•	15.161	15.045	6	•		•	4.	4.	•	13.157	•	•	•	e.	.75	11.498	4.	•	9.194	•	9.224	。	S.	5.9	5.63	16.876	17.114	16.043	15.068	14.087	14.068	15.048	16.016
8.829	•	9.965		•	•	•	7.783	7.672	6.182	5.669	.36	5.968	8.255	8.872	8.112	8.660	8.347	9.222	ö		•		•		14.106	4	•	щ.	12.514	ά.	12.579	3.5	1.75	ο.	10.904	10.887	11.894	11.866		9.826	α
400			400					401		401		401												403					403	403			404		404	4	404	404	404	404	404
LEU ?	•		•	•	LEU A	LEU A	ILE A	-	ILE A		_	ILE A	ILE A	ILE A	SER A	SER A	SER A		SER A			TYR A		TYR A	TYR A		TYR A		TYR A	TYR A	TYR A	TYR A	PHE A	PHE A	PHE A	PHE A	PHE A	PHE A	PHE A	PHE A	PHE A
5	CB	ဗ္ဗ	9	CD2	ບ	0	Z	ව්	g	CG1	6	CG2	ບ	0	z	ð	8	g	บ	0	z	G	æ	ង	9	CEI	CZ	НО	CE2	CD2	ບ	0	z	G	CB	წე	9	CE1	CZ	CE2	9
163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

1122 1112 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 1113 10.19 9.13 8.51 7.79 8.28 7.43 8.17 7.93 7.49 42.617 41.316 38.388 40.929 41.057 40.955 42.061 41.004 39.890 37.583 36.466 35.268 39.670 42.080 42.813 44.505 45.337 44.231 43.373 39.114 41.100 40.027 18.845 19.284 19.284 17.366 20.772 21.036 22.387 22.403 21.698 22.403 23.859 23.150 24.356 23.248 23.248 23.248 24.215 23.974 20.149 18.060 18.036 16.626 16.115 16.823 14.902 18.520 18.526 19.650 20.265 19.165 20.746 20.691 18.050 17.807 17.892 17.817 19.606 16.213 12.255 12.779 14.059 12.832 12.327 12.371 15.190 16.454 16.358 16.101 16.871 16.056 18.163 18.625 20.132 16.155 15.245 PHE A
PHE A
ASN A

o 'z	ບ	0	Z	U	ບ	ບ	ບ	ບ	0	z	U	ບ	ບ	ບ	ບ	Z	U	0	Z	ບ	ບ	ບ	ບ	0	0	ບ	Ó	z	บ	บ	0	ບ	0	Z	ບ	ບ	ບ	O.	יט	ບ
17.24	8.35	7.62	8.01	7.91	6.94	6.32	7.63	.8.05	9.08	8.49	9.75	9.19	. 36.2	0.30	2.28	4.30	0.16	9.72	0.93	2.98	4.77	2.12	0.57	9.00	3.99	0.78	10.26	8.08	6.45	5.87	6.24	99.9	6.05	7.08	9.05	8.83	5.60	2.00	7.75	8.74
000	0	00.	00.	00.	00.	00.	00.	00.	00.	00.	8	00.	.00	00.	00.	00	00.	00.	8.	00.	80.	1.00 2	00.	00.	00.	00.		00.	00.	00.	00.	00.	1.00	•	1.00	1.00	1.00	1.00	1.00 1	1.00
35.930	.02	. 14	.76	.38	.48	.86		32.786	31.569	33.581	33.046	34.066	33.805	34.859	34.478	33.455	31.717	30.884	31.526	30.354		29.569			φ.		28.015	9	œ.	œ.	28.671	7.80	. •	28.836	28.494	9.38	0.44	1.68	28.216	7.67
21.254	21.629	22.453	20.329	19.811	18.525	17.998	19.259	19.497	19.310	19.458	19.154	19.504	18.856	19.221	20.478	20.156							24.221	23.307	25.111	21.398	21.129	21.334	20.831	20.915	22.221	9.3	18.909	18.602	17.282	6.06	.33	15.477	Ŋ	.026
11.027	3.835	3.852	3.848	3.819	4.685	4.357	4.113	.470	.384		.086	.052	.744	.730	.921	.874	.717	766.	.253	.971	335	876	366	.756	827	693	10.082	000	715	174	513	315	313	966	.537	. 925	3.023	.107	12.878	0.274
110	110	410	411	111	411	411	111	411	411	412	412	112	412	412	412	112	112	412	113	113	113	113	113	13	113	113	413	14	14	14	14	14	14	15	415	15	15	415	15	415
ASN A 4		ASN A	ď	ď	Ø	Ø	Ø	Ø		ď	Ø	LYS A 4		LYS A 4	ø	ø	ø	Þ	æ	ø		4	Ø	¥		Ø	ø	ø		SER A 4					Ø	ø	ILE A 4	ø	Ø	ILE A 4
00 ND2	บ	0	Z	ව්	g	ည	8	ບ	0	N	ව්	8	ង	8	B	NZ	ບ	0	z	CA	g	g	8	OE1	OE2	บ	0	z	G	G	90	ບ	0	N	ව්	g	CG1	CD1	CG2	ပ
247	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

0	N	บ	ָט	Ö	ָט	U :	ָט (0 1	Z (ບ	ບ :	י ט	ָט י	ָט י	Z	บ	0	N	υ	.	U	O	z	υ	Z	Z	ט	0	Z	U	ָּט	ט	ָט	υ	0	z	υ	U	บ	ינס	Ö
7.52		7	7.90	11.	11.	'n	_		ហ		ω	_	2	σ	Ŋ	ന	0	N	N	7	വ	M	თ	ω	σ	7		സ	0	7	M	~	n	7	സ	ж. К	9.0	ο.	12.8	18.3	7
	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	-	Н	Н	۲	Н	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
8.	27.974	7.30	8.01	9.45	. 22	29.	25.87	24.90	25.73	24.41	24.53	25	25	24	23		22	24	23	24	23.29	23		26	26	27	22	2		23	2	. 75	ເດ	ä	20.971	2.15	•	1.63	æ	20.530	9.2
-		v	18.514	٥.	19.021	16.647	18.184	17.588	19.286	19.937	21.362	22.296	23.738	24.562	24.843	19.111	18.992	18.424	17.530	17.084	16.222	16.381	16.283	16.901	17.717	16.666	16.374	16.045	15.71	14.671	14.001	щ	•	•	4	Ġ	16.936	18.304	.54		18.239
	9.241	•	6.969	63	. 68	.048	.200	.621	.960	.069	.624	.714	.342	.498	.200	.864	.522	.838	.675	.913	.990	.353	.052	.626	.644	.149	10.873	.026	.022	148	.360	•	•	•	•	7.615	. 7	6.277	•	4.215	ų.
717 K 718	(4	: <	1.EII A 416	: A	Ø	ď	Ą	ø	ø	ø	ø	Ø	ø	ø	ø	ď	ø	Þ	ď	Ø	Ø	ø	ARG A 418	ø	ø	Ø		ø	Ø	ø	ď	ø	Ø	ø	Ø	ø	Ø	ø	LYS A 420	ď	LYS A 420
	· -		5 8																																						CE
0	7 0	2 6	200	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330
**************************************	ALOE &	FOE &	ATOE A	MOT 4	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

. 00 1.00 ..00 16.652 18.957 17.402 16.355 16.190 15.328 14.812 12.022 13.661 18.435 18.902 17.114 16.694 17.722 17.999 19.038 20.397 20.653 16.750 15.923 14.727 14.638 15.166 12.511 13.895 13.371 13.746 12.986 13.576 12.817 14.901 15.558 17.095 17.772 17.825 18.381 18.381 19.548 118.381 15.174 14.845 15.194 14.814 15.256 16.788 13.913 4.073 6.947 10.452 10.452 10.452 10.453 10.453 10.453 10.453 11.11 11.120 11.120 11.120 11.130 11.130 11.1420 11.1420 11.153 12.142 13.031 14.152 15.053 16.653 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 17.152 424 422 422 422 424 425 425 425 425 425 425 333 333 333 333 333 333 333 333 333 340 362 363 364 365 366 367 368 369

111.505 113.661 114.915 114.915 114.915 114.915 115.101 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 117.79 113.013 12.475 110.028 8.882 8.882 8.882 8.882 10.028 11.026 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 11.064 10.494 9.9942 9.9942 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 10.9951 1 ILIE A 426
PHE B 426
PHE B 426
PHE B 426
ILYS A 427
ILYS A 428
GIU A 428
ILYS A 429
ILYS A 429 $\begin{array}{c} \textbf{E} & \textbf{$

	•																							•				•						
8.61 11.42 12.86	. o . v o . d		6 6	4.	e.	0.6		. «	. e.	.8	2.5	6. 9	5.7	ນ ຜິເ	•	4. (2 .	y c) a	•	, d	ין ני איז	9	6.2	6	<u>.</u>	ω 			2.	2	Γ,		38.55
000	888		0 0	000	00.	00.	00.	9 6	• •	00	0	0	0	۰, ۱	1.00	1.00	1.00	9	00.7		> C	7.00	0	1.00	٥.	1.00	1.00	1.00	1.00	1.00			1.00	
4.0	.55	7.77	89.	CJ C	.30	10	. 12	44 C	2 6	14	เง	5.	.70	84	. 78	٠ و	. 74	9 5	. 2	2	7.	4 4 U C	. 92		.08	ന	.07	.75	.66	Φ.	44	. 23		y.
5.450 4.830 3.531	œ 4. /	. 0	നം		8.974	æ	Ξ.			יייי פי	w	2.	4.0	u;	٠.	٠.	۳.	5.439	٠. ١	٠.	Ÿ.	3.571	: -:	٠.	۳.	٠:	3.225	7.	۳.	.75	18	. 53	6.779	N
7.907	32	8.469	.84	טו ני	9 6	4.	3	4.	4	. L	T	۳.	7	7	4	. 7	ហ	2,	9	۰.	₹. '	8.589	. 4	ο.	0.	0.	9	۰.	9	ĸ.	.40	. 95	6.058	.50
A 43 A 43 A 43	A 43 A 43	4 4 4	A 43	4 4	A 43	A 43	A 43		A 43	A 4	< ⊲	A 43	A 43	A 43	A 43	A 43	A 43	A 43	A 43	A 43	A 43	A .	4 4	. 4 4	A 4	ď	A 4	A 43	A 4	A 43	A 4	N A 436	A 4	A
CG PHE CD1 PHE CE1 PHE		CD2 PHE	O PHE	•	ALM ALM	• •	•			CB LYS		CE LYS				•	CA ALA	CB ALA	-							O VAL			C GLY	O GLY	N GLN	CA GILN	CB GLM	CG GIN
415 (416 (417 (۱ ۸۵	m ,	en 18	n w	_	60	σ.	۰,	4 0	1 (1)		Ŋ	w	7	ထ	σ	0	Н	~	43		7 4	47	4	4	ហ	451	ഗ	453	454	455	ហ
ATOM ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM MOTA	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM MOTA	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	· ATOM	ATOM	ATOM

-			•	
40.82 41.74 41.74 34.26 32.88 32.07 31.84 33.28 30.09 28.02 28.75 26.25	# # 0 0 0 0 0 - 0		4 9 8 8 4 9	22.00 16.39 15.75 14.93 13.46 14.00
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			1.00 1.00 1.00 1.00	1.00 1.00 1.00 1.00
-3.115 -3.836 -3.836 0.938 0.952 1.293 2.729 3.330 3.264 4.618 4.591 5.796	4.724 6.426 7.132 7.079 7.079 7.079 8.591	8.749 10.061 9.974 9.051 10.046 7.914	12.283 10.760 11.758 11.088 11.125	11.844 12.555 13.665 11.968 12.581 13.897
6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.064 6.	6.535 6.035 5.035 5.510 6.064	5.952 5.986 6.639 6.142 6.142 5.665	5.193 4.348 3.450 2.105 1.146	1.404 4.004 3.652 5.089 6.399
7.698 8.670 6.778 4.522 2.979 2.979 2.649 1.569 1.569 1.081	0.383 1.680 1.801 3.252 3.330 1.303			3.147 2.832 3.166 3.446 4.514
4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	4 4 4 4 4 4 4 4 6 6 6 6 6 6 6 6 6 6 6 6	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	4 4 4 4 4 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	4441 4441 442 442
GLN GLN GLN GLN GLY GLY GLY GLY GLY GLY GLY GLY GLY GLY	CYS A VAL A VAL A VAL A VAL A VAL A VAL A		HIER HIER CETT	ILE A ILE A ILE A GLY A GLY A
CD OE1 NE2 OC C C C C C C C C C C C C C C C C C C	o z CG1 CG2 CG3	C C C C C C C C C C C C C C C C C C C	G G G G K	C C S O C C C C C C C C C C C C C C C C
44 44 44 44 44 44 44 44 44 44 44 44 44	17444444444444444444444444444444444444	. 4 4 4 4 4 4 4 4 6 6 6 6 6 6 6 6 6 6 6	2 4 4 4 4 4 8 8 8 8 9 9 9 9 9 9 9 9 9 9 9	493 494 495 495 794 898
ATOM ATOM ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM

26.97 32.65 9.95 10.93 10.57 12.33 20.23 27.54 29.64 19.65 16.04 15.05 17.53 20.42 1.00 1.00 1.00 1.00 1.00 000000 00.1 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 17.764 18.558 17.835 18.575 18.559 19.243 19.966 20.558 19.311. 20.978 17.407 17.660 17.337 14.668 12.047 18.236 16.075 17.069 18.097 7.506 18.875 13.790 12.776 12.508 19.354 20.022 6.467 16.821 16.201 15.401 9.145 10.019 10.974 11.916 11.020 1.028 -0.444 3.973 5.593 5.409 3.245 1.909 1.106 3.634 3.836 3.341 1.798 .0.577 4.342 6.634 7.988 9.082 9.103 6.744 4.381 1.987 3.893 2.833 3.765 5.022 5.910 5.318 6.277 6.277 8.564 9.264 8.646 -1.419 -2.048 2.729 5.751 6.220 5.860 6.505 9.472 7.293 6.533 5.895 6.611 1.049 1.074 2.366 2.867 1.407 7.471 5.432 7.190 1.694 0.280 1.153 444 443 444 444 444 ď A A

ບ	ບ	ບ	Z	ບ	0	z	U	ບ	Ö	บ	ບ	U	0	z	ບ	ບ	0	Z	Ö	ບ	ບ	บ	ບ	0	×	บ	ပ	Ö	ບ	Z	ບ.	Z	z	ပ	0	Z	ບ	ບ	Ö	Ö	ບ
													·																												
ω.	2.3	19.61	5.1	0	°	ō.	ø.	r.	6.42	•	•	3.00	•	2.24	3.49	4.47	5.55	3.49	4.55	6.58	7.93	13.08		2.67	2.00	2.00	2.00	2.00	4.	10.15	۰.	13.39	•	2.00		•	2.00	٥.	3.02		Ō
0	1.00	•	1.00	•	•	•	•	•	•	1.00	1.00	1.00	1.00	1.00	•	1.00	•	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	00.	00.	1.00	1.00	00.		1.00	0		0	0	1.00
0	20.456	o,	18.721	.28	.47	. 74	.50	1.6	•	0.48	•	22.949	24.097	•	22.383	23.628	24.600	23.665	24.792	24.875	25.552	23.636				27.117	•		•	•	.27		.82	27.772	8.98	.96	7.44	26.276	4.	25.328	7.93
7.958	00	9.423	.94	•	.80	.35	.21	.9	1.290	. 12	.83	3.501	.19	4.088	4.523	. 42	5.100	.47	7.363	8.319	9.610	8.538	6.676	7.058	5.784	5.160	4.350	5.172	•	5.069	.47	•	15	•	•	•	2.978	•	•	0.419	
•	0.326	•	0.615	4.301	4.442	4.487	•	4.829	٠	49	.88	6.327	6.724	7.089	8.440	8.432	9.127	7.586	7.575	6.399	6.709	5.813	7.157	7.611	6.181	5.688	4.415	3.265	2.114	o.	. 24	98.	-1.326	89	.86	.69	8.787	.49	9.745	0.67	10.172
LYS A 447	A 44	A 44	44	LYS A 447	LYS A 447	Þ	LEU A 448	LEU A 448	æ	Ø		LEU A 448		GLY A 449		GLY A 449	ď	ď		VAL A 450	ď		VAL A 450	ø	Ø			ARG A 451	Ø	Ø		ARG A 451	ARG A 451	æ	ď	ď	A 45	Ø	LEU A 452	LEU A 452	LEU A 452
g	8	뜅	NZ	ບ	0	×	S	8	g	CD1	CD2	ບ	0	z	ð	ບ	0	z	S	CB	CG1	CG2	ပ	0	z	පු	පු	ව්	8	NE	CZ	NHI	NH2	ບ	0	z	đ	GB	Ď	CDI	CDS
144	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	266	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

	•			
2 2 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	40000660		2.58 3.34 3.12 2.58 2.00 6.42 6.42 6.42	2 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
11111111111111111111111111111111111111	00000000			
• • • • • • • • • • • • • • • • • • • •			31.709 32.803 31.388 32.323 31.725 32.471 31.669 33.179	
3.895 3.642 4.944 6.011 7.176 8.535 8.535 9.990	.386 .642 .521 .521 .875 .371	.427 .320 .674 .047 .303	6.274 6.509 3.972 1.507 0.344 0.942	.862 .218 .275 .275 .420 .113
	4000000	7.875 8.888 7.841 7.794 6.795	9.367 9.906 8.890 8.891 8.101 8.180 7.680 7.807	8.348 6.802 10.365 10.681 11.282 12.683 14.859
4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4		. ប៉ូស៊ីសំសំសំសំសំសំ	ហេសសសសសល	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
LEU A 4 IYR A 4	**	**		
				NH1 NH2 C O O CA CB CG1 CG2
7		600 600 600 600 600 600 600 600	607 607 607 610 611 612 613	616 617 618 619 620 621 622 623
ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM

ပင	×	ບ	ບ	บ	Ø	ບ	ບ	0	z	บ	ບ	ບ	บ	0	0	U	0	Z	ບ	ບ	0	บ	0	Z	ບ	່ ບ	ບ	တ	บ	บ	0	×	ט	ับ	บ	บ	ט	່ບ	0	· Þ :
															٠															•										
3.62	2	0		_	2.00			2.00	3.37	4.85	6.22	9.88	w	16.60	H	3.62	2.58	3.61	2.73	0	2.00	3.70	2.47	4.07	4.93	4.86	8.07	13.32	0	5.63	5.63	5.49	ī.	6.42	0	Η.	0		۲.	
1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	00.	00.	1.00	1.00	1.00	1.00	1.00	•	1.00		0.	1.00	1.00.1
32.717	•	3.07	32.443	.04	.57	.70	58	m.		32	36.461	œ	0	39.145	o,	0	38.188	36.300	36.912		36.548	37.168	38.201	36.230	36.433	35.178	33.993	32,523	31,591	37.641	42	37.767	38.821	38.604	37.446	37.283	7	0.21	S	0.3
4.511	76	90	21	45	02	94		9	.54	.48	6.508			6.142	6.470	5.295	5.380	4.189	3.018	1.796	0.633	3.330	2.986	4.020	4.383	5.054	4.164	4.959	3.528	5.320	Η.	•	ņ	.43	44	.33	0.24	6.63	. •	.79
13.432	(1)	w.	щ	•	m.	ω.	13.454		• •		10.250	9.743	8.217	7.728	7.494					13.078				15.368	16.754	17.361	•	œ.		ů.	•	é.	Ġ	5	•	4.	16.678	15.932	99.	
VAL A 456 VAL A 456	A 45	ø	_	MET A 457	MET A 457	ø	MET A 457		Ø	GLU A 458	GLU A 458	ø	ø	ø	GLU A 458	ø	ď		ø		ď	SER A 459	ø	Ø	MET A 460	ø	ď	ď,	MET A 460	ø	¥	ď	ď	ď	A	A 4	LEU A 461	LEU A 461		ď
ပဝ	×	g	CB	g	SD	S	ບ	0	z	ð	CB	ង្គ	8	OE1	OE2	ບ	0	z	ð	9	90	ບ	0	×	ජ	ප								•			CD 7	ر ت	0	E E
625	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	629	099	199	ဖ	663	9		999
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

14.00 24.00 13.37 15.00 13.58 17.87 15.03 13.80 18.04 17.67 19.26 20.75 1.00 14.52 1.00 15.99 14.97 1.00 13.63 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 44.428 44.544 42.533 39.072 42.729 46.085 45.086 45.554 46.552 46.399 41.628 43.107 47.260 46.301 40.971 41.321 39.244 39.965 38.654 43.440 45.889 45.356 6.509 6.526 6.362 6.619 7.176 7.574 8.431 8.538 8.543 6.218 3.978 2.740 1.391 4.958 8.192 2.995 2.288 3.479 5.767 6.912 5.003 6.627 4.922 0.404 3.733 21.027 22.427 22.561 23.388 20.064 21.057 18.835 18.551 17.056 14.653 13.464 12.086 10.931 9.546 16.346 16.346 17.684 17.684 18.055 19.089 19.009 20.196 15.185 14.733 18.257 18:800 17.805 17.638 20.600 14.460 18.818 SER A 463
SER A 463
SER A 463
SER A 463
GLU A 464
GLU A 464
GLU A 464
GLU A 464
GLU A 465
GLU A 465 A 463 462 695 696 697 698 669 675 678 619 680 681 682 683 684 685 686 687 688 689 690 691 692 693 694 700

.

.

.

O I	ບ	ບົ	ບ	Z	บ	×	Z	บ	0	¤	O	Ċ	ບ	U	บ	υ	0	N	ບ	ט	0	ບ	0	Z	บ	ບ	ပ	ပ	O	ບ	0	z	Ö	ບ	ບ	ບ	0	Z	ט	0	N	•	
0 24.4	.00 23.4	.00 21.8	.00	.00 18.6	.00 15.7	.00 12.8	.00 18.	.00 24.2	.00 25.	.00 23.	.00 23.	.00 23.	.00 23,	.00 19.	.00 25.	.00 24.	.00 23.	.00 24.	.00 25.	.00 26.	00 24.	00 26.	00 28.	00 26.	00 25.	00 25.	00 26.	00 28.	00 25.	00 25	00 23.6	00 26.3	00 27.7	00 28.6	00 32.7	00 38.9	00 36.4	00 41.4	8	00 28.3	0 25.5		
N.	43.576	43.224	41.707	41.616	40.982	40.281	41.027	45.573	45.988	45.572	45.983	44.801	43.581	42.390	43.836	47.087	47.608	47.427	48.310	49.621	50.339	47.500	46.285	48.091	47.218	46.458	47.112	46.636	44.944	46.260	υ,	6.17	5.21	5.83	. 72	48.043	.84	48.257	44.141	.77	43.585	٠	
3.659	46	Ġ	3.512	۰.	۰.	۲.	4.	4.765	ιú	5.979	7.109	8.052	7.685	8.459	8.047	7.919		7.549	8.357		7.352	9.644		10.774	11.941	12.106	24	42	31	81	0.76	.87	89	.38	.37	.08	0	ω.	13.851	13.799	. 7		
22.666	92	35	65	10	36	25.481	64	23.560	24.669	23.067	23.871	24.092	24.921	24.393	26.380	23.174	23.753	21.940	21.160	21.893	22.034	21.022	21.227	20.666	20.567	21.907	22.706	24.137	તં	19.406	19.196	18.600	-	2	Ŋ.	ė	6.53	6.65	8.00	19.174	v		
A 4	4	•	ARG A 467	ARG A 467	A 4	ARG A 467	ARG A 467	ARG A 467	4	ď	ø		LEU A 468	ø;	ø	LEU A 468	Ø	ø	ď	SER A 469	ø	ø	ø	ø	ď	Ø	-	ø	ø	-	Ø	ď	æ	-		¥	Ø	GLN A 471	Ø	GLN A 471	ASN A 472		
ð	9	ပ္ပ	8	NE	Z	NH1	NH2	บ	0	×	ð	8	នួ	CD	CD5	U	0	z	ర	9	90							CD				_	-	9	_		OE1 (υ	0	N N		
709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	4	746	4	748	749	750		
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM		

Ö	ັ	O	0	z	U	0	Z	ŭ	ບ	ט	ט	O	ŭ	Ö	ט	ບ	0	Z	Ö	U	o	U	0	Z	ບ	ບ	ບ	บ	ບ	N	O	С	•	Z	OBO	OBOO	0000	00000	. x 0 0 0 0 0	. ¤ 0 0 0 0 0 0
.00 25	.00 24	.00 28	.00 23	.00 29	.00 22	.00 21	.00 19	.00 17.	.00 15	.00 14	.00 14	.00 11.	.00	.00 10.	.00 13,	.00 15.	.00 15,	.00 13.	.00 13	.00 14.	.00 6.	.00 13.	.00 13.	.00 13.	.00 12.	.00 12.	.00 13.	.00 16.	.00 24.	.00 23.	.00 12.	.00 14.	.00 12.		.00 11.	00 11.	00 11.	.00 11. .00 14.	00 11.	00 11. 00 14. 00 12. 00 14.
.68	.34	.70	9	.39	. 25	0.44	0.99	. 65	9.17	0.04	.03	96.	1.78	0.81	9.95	8.52	7.36	œ.	7	œ.	7	ů.	'n.	Ġ.	5.75	6.18	5.03	5.48	4.3I	2.93	4.74	3.53	5.20		4.29	4.29 5.05	4.29 6.29 7.03 7.03	4.29 5.05 4.25 3.21	8 3 4 5 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	4 4 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6
. 73	.42	7.80	8.68	7.97	5.19	.90	5.04	.53	.27	.09	11.788	10.715	9.961	10.257	11.329	15.623	15.264	16.910	18.016	19.379	20.550	17.877	18.062	17.578	17.435	17.089	17.204	17.423	17.332	18.006	16.436	16.736	15.223	701 71	# 7 T . T T	12.879	12.879 11.659	12.879 11.659 11.262	12.879 11.659 11.262 10.436	12.879 11.659 11.262 10.436
.75	.98	.34	.87	.07	.11	4	.41	.88	-	•	-	18.603	19.726	20.648	20.444	19.944	20.018	19.930	19.840	20.136	19.705	20.702	20.221	21.978	22.878	24.286	25.288	26.724	4	0	9	m	ထ	~	•	9	0 5	0 7 0	0000	00000
4	A 4	A 4	ď	Ø	¥	ø	Ø	ø	ď	Ø	Ø	Ø	ø	ø	Ķ	Ø	ø	ø	ď	Ø	ď	ď	ď	Ø	ď	ď	ø	Ø	æ	Ø	Ø	¥	ď	ď		Ø	44	444	**	**
	•				•	O AS	N PE																																· · · · · · · · ·	· · · · · · · · · · · · · · · · · · ·
751	752	753	754	755	756	757	758	759	760	761																														
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM		ATOM	ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM ATOM
752 CB ASN A 472 18.385 16.425 43.345 1.00 24 753 CG ASN A 472 19.348 17.803 42.708 1.00 23 754 OD1 ASN A 472 19.073 118.682 43.391 1.00 23 755 C ASN A 472 19.073 118.682 43.391 1.00 23 756 C ASN A 472 19.073 118.682 43.391 1.00 23 757 O ASN A 472 19.073 118.682 43.391 1.00 23 758 N PHE A 473 19.419 15.043 40.946 1.00 19 759 CR PHE A 473 19.095 13.278 39.175 1.00 19 760 CR PHE A 473 19.095 13.278 39.175 1.00 19 761 CG PHE A 473 19.095 13.278 39.175 1.00 19 762 CD PHE A 473 19.095 13.278 39.175 1.00 15 764 CD PHE A 473 19.095 13.278 39.175 1.00 15 765 CE PHE A 473 19.095 13.278 39.175 1.00 15 766 CE PHE A 473 19.095 13.278 39.175 1.00 15 767 C PHE A 473 19.095 13.278 39.175 1.00 15 768 CE PHE A 473 19.095 13.278 39.954 1.00 13 769 N SER A 474 19.930 16.910 38.897 1.00 13 770 C SER A 474 20.013 15.264 10.00 13 771 CB SER A 474 20.013 15.264 1.00 13 772 C SER A 474 20.013 16.910 38.897 1.00 13 773 C SER A 474 20.702 17.877 36.691 1.00 13 774 O SER A 475 20.221 18.062 35.754 1.00 13 775 C SER A 475 20.221 18.062 35.754 1.00 13 776 CB IXS A 475 20.221 18.062 35.754 1.00 13 777 CB IXS A 475 20.221 18.062 35.754 1.00 13 778 CB IXS A 475 20.221 18.062 35.754 1.00 13 779 CB IXS A 475 20.221 18.062 35.754 1.00 12 778 CB IXS A 475 20.247 17.432 35.480 1.00 13 779 CB IXS A 475 20.247 17.432 35.480 1.00 13 779 CB IXS A 475 20.247 17.023 35.480 1.00 12 780 CB IXS A 475 20.247 17.023 35.480 1.00 12 781 NG IXS A 475 20.247 17.623 35.293 1.00 12 782 CB IXS A 475 20.408 16.736 33.530 1.00 12 784 NG IEU A 476 20.272 11.659 34.724 1.00 12 785 CB IEU A 476 20.059 10.247 33.231 1.00 13 786 CB IX A 475 20.247 10.047 35.033 1.00 14 786 CB IX A 475 20.247 10.243 35.050 1.00 14 787 CB IX A 475 20.444 33.520 1.00 14 788 CB IX A 476 20.271 18.045 35.253 1.00 14 789 CB IX A 476 20.271 18.050 33.212 1.00 14 789 CB IX A 476 20.271 18.04 35.031 1.00 11 789 CB IX A 476 20.272 11.659 34.225 1.00 11 780 CB IX A 476 20.272 11.659 34.225 1.00 11 780 CB IX A 476 20.272 11.659 34.225 1.00 11 780 CB IX A 476 20.272 11.650 35.233 1.00 11 780 CB IX A 4	753 CG ASN A 472 19.348 17.803 42.708 1.00 28.30 754 OD1 ASN A 472 19.877 118.682 43.390 1.00 23.38 755 CA ASN A 472 19.673 17.974 41.391 1.00 22.63 756 C ASN A 472 19.118 15.198 41.256 1.00 22.63 757 O ASN A 472 19.118 15.198 41.256 1.00 22.63 758 N PHE A 473 19.491 15.492 40.996 1.00 19.00 759 O BN A 473 19.491 15.494 10.00 14.08 760 CB PHE A 473 19.095 13.278 39.175 1.00 14.58 761 CG PHE A 473 19.095 13.278 39.175 1.00 14.58 762 CB1 PHE A 473 19.095 13.278 39.175 1.00 14.58 763 CB1 PHE A 473 19.726 9.961 41.708 1.00 11.36 764 CZ PHE A 473 19.726 9.961 41.708 1.00 11.36 765 CB2 PHE A 473 19.726 9.961 41.708 1.00 11.36 766 C PHE A 473 19.944 11.329 39.954 1.00 13.40 767 C PHE A 473 19.944 11.329 39.954 1.00 13.40 770 C PHE A 474 19.840 18.016 37.366 1.00 13.47 771 CB SER A 474 19.840 18.016 37.387 1.00 13.47 772 CG SER A 474 20.702 17.877 36.691 1.00 13.47 774 C SER A 474 20.702 17.877 36.691 1.00 13.47 775 CB LYS A 475 20.702 17.877 36.691 1.00 13.47 776 CB LYS A 475 20.702 17.877 36.691 1.00 13.47 777 CB LYS A 475 20.702 17.878 36.867 1.00 13.47 778 CG LYS A 475 22.4286 17.089 36.185 1.00 12.77 779 CD LYS A 475 22.4286 17.089 36.185 1.00 12.77 779 CD LYS A 475 22.4286 17.089 36.185 1.00 12.77 779 CD LYS A 475 22.428 17.323 35.233 1.00 12.77 779 CD LYS A 475 22.428 17.204 35.033 1.00 12.77 779 CD LYS A 475 22.428 17.204 35.037 1.00 12.77 779 CD LYS A 475 22.428 17.204 35.037 1.00 12.77 779 CD LYS A 475 22.428 17.204 35.037 1.00 12.77 779 CD LYS A 475 22.428 17.204 35.037 1.00 12.77 770 CD LYS A 475 22.428 17.204 35.037 1.00 12.77 771 CD LYS A 475 22.428 17.204 35.037 1.00 12.77 770 CD LYS A 475 22.428 17.204 35.037 1.00 12.77 771 CD LYS A 475 22.428 17.205 33.510 1.00 12.77 772 CD LYS A 475 22.428 17.205 33.510 1.00 12.77 774 CD LYS A 475 22.428 17.205 33.520 1.00 12.77 775 CD LYS A 475 22.428 17.205 33.520 1.00 12.77 776 CD LYS A 476 22.188 16.736 32.537 1.00 12.77 777 CD LYS A 476 22.188 16.736 32.537 1.00 12.77 778 CD LYS A 476 22.188 15.223 35.203 1.00 12.77 779 CD LYS A 476 22.188 15.223 35.203 1.00 12.1	754 ODJ ASN A 472 19.877 18.662 43.390 1.00 23.38 755 ND2 ASN A 472 19.073 17.974 41.391 1.00 29.62 756 ND2 ASN A 472 19.073 17.974 41.391 1.00 22.63 757 C ASN A 472 11.204 14.902 40.466 1.00 21.63 759 CA PHE A 473 19.419 15.043 40.990 1.00 19.00 759 CA PHE A 473 19.419 15.043 40.990 1.00 19.00 759 CA PHE A 473 19.695 13.278 39.175 1.00 14.08 762 CD1 PHE A 473 19.095 13.278 39.175 1.00 14.53 762 CD1 PHE A 473 19.295 12.095 40.041 1.00 14.08 764 CZ PHE A 473 19.295 11.788 41.001 1.00 14.53 765 CZ PHE A 473 19.295 11.789 41.001 1.00 14.53 765 CZ PHE A 473 19.295 11.789 11.785 1.00 13.01 765 CZ PHE A 473 19.295 10.257 40.810 1.00 11.36 765 CZ PHE A 473 19.295 10.257 40.810 1.00 13.01 765 CZ PHE A 473 19.295 10.257 40.810 1.00 13.72 770 CS PHE A 474 19.290 16.910 81.897 770 CS PHE A 474 19.290 16.910 81.897 770 CS PHE A 474 20.136 19.379 38.604 1.00 13.72 770 CS PHE A 474 20.136 19.379 38.604 1.00 13.49 770 CS PHE A 474 20.136 19.379 38.604 1.00 13.49 770 CS PHE A 474 20.121 18.052 35.597 1.00 13.49 770 CS PHE A 474 20.121 18.052 35.397 1.00 13.49 770 CS PHE A 474 20.121 18.052 35.397 1.00 13.49 770 CS PHE A 475 20.221 18.052 35.397 1.00 13.49 770 CS PHE A 475 20.221 18.052 35.397 1.00 13.49 770 CS PHE A 475 20.221 18.00 22.357 1.00 13.49 770 CS PHE A 475 20.221 18.00 22.357 1.00 13.49 770 CS PHE A 475 20.221 18.00 35.78 1.00 12.47 770 CS PHE A 475 22.486 17.089 36.185 1.00 12.47 770 CS PHE A 475 22.487 17.204 35.037 1.00 12.47 770 CS PHE A 475 22.487 17.204 35.037 1.00 12.47 770 CS PHE A 475 22.487 17.204 35.037 1.00 12.47 770 CS PHE A 475 22.487 17.204 35.037 1.00 12.47 770 CS PHE A 475 22.487 17.204 35.037 1.00 12.47 770 CS PHE A 475 22.487 17.204 35.037 1.00 12.47 770 CS PHE A 475 22.487 17.204 35.233 1.00 12.47 1.00 12.47 78 CS PHE A 475 22.487 17.207 35.537 1.00 12.47 78 CS PHE A 475 22.487 17.207 35.537 1.00 12.47 78 CS PHE A 475 22.487 17.207 35.531 1.00 12.47 78 CS PHE A 475 22.487 16.208 36.188 17.204 17.00 12.47 17.00 12.47 17.00 12.47 17.00 12.47 17.00 12.47 17.00 12.47 17.00 12.47 17.00 12.47 17.00 12.	755 ND2 ASN A 472 19.073 17.974 41.391 1.00 22.82 756 C ASN A 472 17.204 14.902 40.446 1.00 22.63 758 N PHE A 473 19.419 15.043 40.996 1.00 12.03 759 CA PHE A 473 19.429 15.043 40.996 1.00 12.03 750 CB PHE A 473 19.095 13.278 39.175 1.00 15.51 762 CD PHE A 473 19.295 12.095 40.041 1.00 14.08 763 CES PHE A 473 19.295 12.095 40.041 1.00 14.08 764 CZ PHE A 473 19.295 12.095 40.041 1.00 14.53 765 CES PHE A 473 19.295 12.095 40.041 1.00 14.53 765 CES PHE A 473 19.295 12.095 40.041 1.00 14.53 765 CES PHE A 473 19.726 10.715 41.900 1.00 11.36 765 CES PHE A 473 19.295 12.095 40.010 1.00 10.92 766 CD PHE A 473 19.295 10.715 41.900 10.01.30 770 C PHE A 473 20.444 11.329 39.954 1.00 13.01 771 CB SER A 474 19.390 16.910 38.897 1.00 13.72 772 C SER A 474 19.390 16.910 38.897 1.00 13.74 774 O SER A 474 20.702 17.877 36.691 1.00 13.49 775 C SER A 474 20.702 17.877 36.691 1.00 13.49 776 CB LYS A 475 22.878 17.578 36.867 1.00 13.49 777 CB LYS A 475 22.878 17.52 35.597 1.00 13.49 778 CG LYS A 475 22.878 17.204 35.033 1.00 13.73 779 CB LYS A 475 22.878 17.204 35.033 1.00 13.73 770 CB LYS A 475 22.878 17.204 35.033 1.00 13.73 771 CB LYS A 475 22.878 17.204 35.033 1.00 12.47 772 CB LYS A 475 22.878 17.204 35.033 1.00 12.47 773 CB LYS A 475 22.878 17.204 35.033 1.00 12.47 774 CB LYS A 475 22.878 17.204 35.033 1.00 12.47 775 CB LYS A 475 22.878 17.204 35.033 1.00 12.47 776 CB LYS A 475 22.488 17.204 35.031 1.00 12.47 777 CB LYS A 475 22.488 17.204 35.031 1.00 12.47 778 CG LYS A 475 22.488 17.204 35.031 1.00 12.47 779 CB LYS A 475 22.488 17.204 35.031 1.00 12.47 786 CB LYS A 475 22.488 17.204 35.031 1.00 12.84 786 CB LEU A 476 22.188 15.224 35.030 1.00 14.20 787 CD LYS A 475 22.488 15.225 1.00 12.84 788 CD1 LEU A 476 22.188 15.225 1.00 12.84 789 CD LYS A 475 20.99 10.436 35.250 1.00 14.10 780 CD LYS A 476 22.189 15.23 35.250 1.00 12.87 780 CD LYS A 475 20.899 10.436 33.212 1.00 12.158 780 CD LYS A 476 22.88 16.248 17.204 33.212 1.00 12.84 780 CD LYS A 476 22.89 14.44 33.234 1.00 12.17	756 C ASN A 472 18.118 15.188 41.256 1.00 22.63 757 O ASN A 472 17.204 14.902 40.446 1.00 22.63 758 CA PER A 473 19.485 14.539 39.654 1.00 19.00 759 CA PER A 473 19.485 14.539 39.654 1.00 17.56 761 CG PER A 473 19.095 13.278 39.175 1.00 14.53 762 CED PER A 473 19.295 13.278 39.175 1.00 14.53 763 CED PER A 473 18.503 10.715 41.900 1.00 11.36 764 CZ PER A 473 18.603 10.715 41.900 1.00 11.36 765 CE PER A 473 19.726 9.961 41.785 1.00 13.01 766 CD PER A 473 19.946 10.257 40.80 1.00 13.01 767 C PER A 473 19.946 10.257 40.80 1.00 13.01 768 O PER A 474 19.940 18.063 10.01 3.01 770 CS SER A 474 20.136 19.379 38.697 1.00 13.01 771 CB SER A 474 20.136 19.39 39.649 1.00 13.44 772 CG SER A 474 20.136 19.39 38.671 1.00 13.41 774 CB SER A 474 20.136 19.37 38.691 1.00 13.41 775 CG SER A 475 20.21 18.062 35.597 1.00 13.47 776 CB SER A 475 20.21 18.062 35.597 1.00 13.47 777 CB SER A 475 20.21 18.062 35.597 1.00 13.47 778 CG SER A 475 20.2878 17.204 35.03 1.00 13.47 779 CB SER A 475 20.2878 17.578 36.691 1.00 13.37 770 CB SER A 475 20.2878 17.578 36.691 1.00 13.37 777 CB SER A 475 20.2878 17.578 36.691 1.00 13.47 778 CG SER A 475 20.2878 17.578 36.691 1.00 13.47 779 CB SER A 475 20.2878 17.204 35.037 1.00 12.47 770 CB SER A 475 20.2878 17.578 36.691 1.00 13.49 777 CB SER A 475 20.2878 17.578 36.691 1.00 12.47 778 CG SER A 475 20.2878 17.204 35.037 1.00 12.47 779 CB SER A 475 20.467 16.435 35.754 1.00 12.94 770 CB SER A 475 20.467 16.435 35.480 1.00 12.94 770 CB SER A 475 20.467 16.436 32.937 1.00 12.94 771 CB SER A 476 20.188 15.223 35.203 1.00 14.20 772 CB SER A 476 20.188 15.223 35.00 1.00 14.20 773 CB SER A 476 20.188 15.223 35.00 1.00 14.20 774 CB SER A 476 20.189 15.225 35.00 1.00 12.94 775 CB SER A 476 20.189 15.225 33.512 1.00 12.97 770 CB SER A 476 20.035 14.44 33.512 1.00 11.58 770 CB SER A 476 20.035 14.44 33.512 1.00 11.58	757 O ASN A 472 17.204 14.902 40.446 1.00 21.83 758 N PHE A 473 19.885 14.592 40.695 1.00 19.00 759 N PHE A 473 19.885 14.593 9.654 1.00 17.56 760 CB PHE A 473 19.095 13.278 39.175 1.00 15.51 761 CG PHE A 473 19.095 13.278 39.175 1.00 15.51 762 CD1 PHE A 473 19.095 13.278 40.041 1.00 14.63 763 CED PHE A 473 19.726 9.961 41.785 1.00 13.01 764 CZ PHE A 473 19.726 9.961 41.785 1.00 18.01 765 CED PHE A 473 19.726 9.961 41.785 1.00 13.01 766 CD PHE A 473 19.726 9.964 10.01 1.36 766 CD PHE A 473 19.726 9.964 10.01 1.36 767 C PHE A 473 19.726 9.964 10.01 15.68 768 O PHE A 473 19.726 9.964 10.01 15.68 770 CB SER A 474 19.705 20.593 38.897 1.00 13.72 771 CB SER A 474 20.136 19.39 38.694 1.00 13.74 772 CG SER A 474 20.136 19.39 38.694 1.00 13.44 774 CB SER A 474 20.136 19.39 38.691 1.00 13.37 775 CB SER A 475 20.21 17.873 36.591 1.00 13.37 776 CB SER A 475 22.878 17.204 35.033 1.00 13.37 777 CB SER A 475 22.878 17.204 35.033 1.00 13.37 778 CG SER A 475 22.878 17.204 35.033 1.00 13.37 779 CB SER A 475 22.878 17.204 35.033 1.00 13.37 770 CB SER A 475 22.878 17.204 35.033 1.00 13.73 771 CB SER A 475 22.878 17.204 35.033 1.00 13.73 772 CB SER A 475 22.878 17.204 35.033 1.00 12.47 774 CB SER A 475 22.878 17.204 35.033 1.00 12.47 775 CB SER A 475 22.878 17.204 35.033 1.00 12.84 776 CB SER A 475 22.467 18.06 32.937 1.00 12.94 777 CB SER A 475 22.467 18.06 32.937 1.00 12.94 778 CG SER A 475 22.467 18.06 32.937 1.00 12.84 780 CB SER A 475 22.467 18.06 32.937 1.00 12.84 781 CB SER A 476 22.188 15.223 35.203 1.00 12.84 782 C SER A 476 22.188 15.223 35.203 1.00 12.84 783 CD SER A 476 22.188 15.223 35.203 1.00 12.84 784 N SER A 476 22.188 15.223 35.203 1.00 14.82 785 CD SER A 476 22.188 15.223 35.203 1.00 12.84 786 CD SER A 476 22.188 15.223 35.203 1.00 12.84 787 CD SER A 476 22.188 15.223 35.203 1.00 12.84 788 CD SER A 476 22.099 11.262 33.212 1.00 14.10 789 CD SER A 476 22.099 11.262 33.212 1.00 14.10	758 N PHE A 473 19.419 15.043 40.990 1.00 19.00 759 CB PHE A 473 19.485 14.539 39.654 1.00 17.56 760 CB PHE A 473 19.495 13.278 39.175 1.00 14.08 762 CD PHE A 473 19.295 12.095 40.041 1.00 14.08 762 CD PHE A 473 19.295 12.095 40.041 1.00 14.08 764 CZ PHE A 473 19.726 9.961 41.031 1.00 14.08 765 CD PHE A 473 20.648 10.257 40.810 1.00 11.36 765 CD PHE A 473 20.648 10.257 40.810 1.00 10.92 766 CD PHE A 473 20.648 10.257 40.810 1.00 10.92 766 CD PHE A 473 20.648 10.257 40.810 1.00 13.01 767 C PHE A 473 20.644 11.329 39.954 1.00 13.01 768 O PHE A 473 20.648 10.257 40.810 1.00 13.01 770 CA SER A 474 19.940 16.916 37.936 1.00 13.72 771 CB SER A 474 20.702 17.877 36.694 1.00 13.44 772 C SER A 475 20.136 19.379 38.604 1.00 13.44 774 C SER A 475 20.136 19.379 36.867 1.00 13.47 775 M LYS A 475 22.878 17.578 36.867 1.00 13.47 776 CA LYS A 475 22.878 17.287 35.784 1.00 13.73 779 CD LYS A 475 22.878 17.283 35.784 1.00 12.47 777 CB LYS A 475 22.428 17.283 35.480 1.00 12.47 778 CG LYS A 475 22.428 17.283 35.480 1.00 12.47 779 CD LYS A 475 22.428 17.283 35.480 1.00 12.47 779 CD LYS A 475 22.426 11.029 36.185 1.00 12.47 779 CD LYS A 475 22.426 11.02 13.93 779 CD LYS A 475 22.440 18.063 32.337 1.00 13.73 780 CB LYS A 475 22.440 18.063 32.337 1.00 13.73 781 LYS A 475 22.440 18.043 33.530 1.00 14.20 785 CA LYS A 476 22.440 18.063 32.337 1.00 12.84 786 CB LYS A 476 21.567 12.879 35.203 1.00 14.20 787 CG LYS A 476 21.671 12.473 35.203 1.00 11.55 788 CD LIEU A 476 21.677 12.879 35.250 1.00 14.10 789 CD LYS A 476 21.671 12.474 33.512 1.00 12.77 789 CD LYS A 476 20.099 11.262 33.212 1.00 11.57 780 CD LYS A 476 20.099 11.262 33.212 1.00 11.57 780 CD LYS A 476 21.099 11.262 33.212 1.00 11.57 780 CD LYS A 476 20.099 11.262 33.212 1.00 11.57 780 CD LYS A 476 20.099 11.262 33.212 1.00 11.57 780 CD LYS A 476 20.099 11.262 33.212 1.00 11.57 780 CD LYS A 476 20.099 11.262 33.212 1.00 11.57 780 CD LYS A 476 20.099 11.262 33.212 1.00 11.57 780 CD LYS A 476 20.099 11.262 33.212 1.00 11.20 780 CD LYS A 476 20.099 11.262 33.212 1.00 11.20	759 CA PHE A 473 19.885 14.539 39.654 1.00 17.56 760 CB PHE A 473 19.295 12.095 40.041 1.00 14.53 761 CG PHE A 473 19.295 12.095 40.041 1.00 14.53 762 CD1 PHE A 473 18.379 11.788 41.031 1.00 14.53 764 CZ PHE A 473 18.726 3.0514 1.00 1.00 11.36 765 CG2 PHE A 473 19.726 9.961 41.785 1.00 13.01 765 CG2 PHE A 473 20.444 11.329 39.954 1.00 13.01 767 C PHE A 473 20.444 11.329 39.954 1.00 13.01 768 O PHE A 473 20.444 11.329 39.954 1.00 13.01 769 N SER A 474 19.940 18.016 37.936 1.00 13.01 770 CA SER A 474 19.940 18.016 37.936 1.00 13.17 771 CB SER A 474 20.136 19.379 38.604 1.00 13.49 772 C SER A 474 20.136 19.379 36.691 1.00 13.44 774 C SER A 474 20.221 18.062 35.597 1.00 13.49 775 CA IXX A 475 22.2878 17.578 36.867 1.00 13.49 776 CA IXX A 475 22.2878 17.204 35.031 1.00 13.47 778 CG IXX A 475 22.2878 17.204 35.391 1.00 13.47 779 CB IXX A 475 22.2878 17.204 35.391 1.00 13.47 779 CB IXX A 475 22.2878 17.204 35.033 1.00 13.47 779 CB IXX A 475 22.2878 17.204 35.033 1.00 13.47 779 CB IXX A 475 22.2878 17.204 35.037 1.00 13.47 779 CB IXX A 475 22.288 17.204 35.038 1.00 12.47 779 CB IXX A 475 22.288 17.204 35.038 1.00 12.66 780 CE IXX A 475 22.467 16.436 34.477 1.00 12.94 781 NZ IXX A 475 22.467 16.436 34.477 1.00 12.94 782 C IXX A 476 22.487 10.01 2.94 785 CB IXW A 476 22.188 15.223 35.203 1.00 11.55 786 CB IXW A 476 21.567 12.879 34.254 1.00 11.57 787 CB IXW A 476 21.979 11.262 33.212 1.00 11.57 789 CD IXW A 476 21.999 11.262 33.212 1.00 11.57 789 CD IXW A 476 20.999 11.262 33.212 1.00 11.57 789 CD IXW A 476 20.999 11.262 33.212 1.00 11.57 789 CD IXW A 476 20.999 11.262 33.212 1.00 11.57 789 CD IXW A 476 20.999 11.262 33.212 1.00 11.57 789 CD IXW A 476 20.999 11.262 33.212 1.00 11.57 789 CD IXW A 476 20.999 11.262 33.212 1.00 11.57	760 CB PHE A 473 19.095 13.278 39.175 1.00 15.51 761 CG PHE A 473 19.295 12.095 40.041 1.00 14.08 762 CD1 PHE A 473 18.603 10.715 41.900 1.00 14.08 763 CE1 PHE A 473 18.603 10.715 41.900 1.00 14.53 765 CE2 PHE A 473 19.726 9.961 10.00 1.36 766 CD2 PHE A 473 20.648 10.257 40.810 1.00 10.92 766 CD2 PHE A 473 20.648 10.257 40.810 1.00 10.92 768 CD2 PHE A 473 20.048 11.329 39.954 1.00 13.01 769 N SER A 474 19.930 16.910 38.897 1.00 15.69 770 CA SER A 474 19.840 18.016 37.936 1.00 13.72 771 CB SER A 474 20.221 18.062 35.597 1.00 13.44 774 O SER A 475 20.221 18.062 35.597 1.00 13.49 775 C SER A 475 20.221 18.062 35.597 1.00 13.49 776 CA LYS A 475 21.978 17.578 36.691 1.00 13.49 777 CB LYS A 475 21.978 17.578 36.891 1.00 13.49 778 CG LYS A 475 21.978 17.578 36.807 1.00 13.49 779 CD LYS A 475 22.286 17.204 35.033 1.00 13.77 779 CD LYS A 475 22.286 17.204 35.033 1.00 13.77 779 CD LYS A 475 22.288 17.204 35.033 1.00 13.77 779 CD LYS A 475 22.288 17.204 35.03 1.00 12.47 777 CB LYS A 475 22.288 17.204 35.03 1.00 13.73 779 CD LYS A 475 22.288 17.204 35.03 1.00 13.73 779 CD LYS A 475 22.288 17.204 35.03 1.00 13.73 779 CD LYS A 475 22.288 17.204 35.03 1.00 13.73 780 CB LYS A 475 22.288 17.204 35.03 1.00 12.94 781 N LEU A 476 22.188 15.223 35.203 1.00 14.20 782 CB LYS A 475 22.488 16.736 33.530 1.00 14.20 783 CD LYS A 476 21.899 11.262 33.212 1.00 14.10 784 CD LYS A 476 21.892 14.412 33.514 1.00 11.57 785 CD LYS A 476 21.892 11.859 35.289 1.00 11.57 786 CD LYS A 476 21.892 11.262 33.212 1.00 14.10 787 CD LYS A 476 21.892 11.262 33.212 1.00 14.10 788 CD LYS A 476 21.892 11.262 33.212 1.00 14.10 789 CD LYS A 476 21.892 11.262 33.212 1.00 14.10 789 CD LYS A 476 21.892 11.262 33.212 1.00 14.10 780 CD LYS A 476 21.892 11.262 33.212 1.00 14.10 780 CD LYS A 476 21.892 11.262 33.212 1.00 14.10 780 CD LYS A 476 21.892 11.262 33.212 1.00 14.10 780 CD LYS A 476 21.892 11.444 33.514 1.00 11.57	761 CG PHE A 473 19.295 12.095 40.041 1.00 14.08 762 CD1 PHE A 473 18.379 11.788 41.031 1.00 14.53 765 CD2 PHE A 473 19.726 9.961 41.785 1.00 8.01 765 CD2 PHE A 473 20.644 11.329 39.954 1.00 13.01 767 C PHE A 473 20.644 11.329 39.954 1.00 13.01 768 O PHE A 473 20.644 11.329 39.954 1.00 13.01 767 C PHE A 473 20.644 11.329 39.954 1.00 13.01 768 O PHE A 473 20.018 15.264 37.360 1.00 15.69 769 N SER A 474 19.940 16.910 38.897 1.00 13.01 770 CB SER A 474 19.940 18.016 37.936 1.00 14.23 771 CB SER A 474 20.136 19.379 38.604 1.00 14.23 772 CG SER A 474 20.136 19.379 38.604 1.00 14.23 774 O SER A 474 20.136 19.379 38.604 1.00 13.44 775 CB LYS A 475 20.287 17.877 36.691 1.00 13.49 776 CA LYS A 475 22.878 17.268 35.861 1.00 13.47 777 CB LYS A 475 22.878 17.204 35.754 1.00 12.47 778 CG LYS A 475 22.878 17.204 35.734 1.00 12.47 779 CD LYS A 475 22.878 17.204 35.735 1.00 12.47 779 CD LYS A 475 22.487 17.203 36.481 1.00 12.47 779 CD LYS A 475 22.487 17.203 35.480 1.00 12.47 777 CB LYS A 475 22.487 17.204 35.754 1.00 12.47 777 CB LYS A 475 22.487 17.204 35.754 1.00 12.47 777 CB LYS A 475 22.487 17.204 35.754 1.00 12.47 777 CB LYS A 475 22.487 17.203 36.185 1.00 12.47 777 CB LYS A 475 22.487 10.01 2.47 777 CB LYS A 475 22.487 10.01 2.47 777 CB LYS A 475 22.487 10.01 12.00 12.77 789 C LYS A 475 22.48 16.736 34.747 1.00 12.94 780 C LYS A 475 22.48 16.736 34.747 1.00 12.94 781 NEU A 476 22.188 15.223 35.291 1.00 14.10 789 C LYS A 476 21.999 11.262 33.212 1.00 14.10 780 C LEU A 476 21.999 11.262 33.212 1.00 14.10 780 C LEU A 476 21.999 11.262 33.212 1.00 14.10 780 C LEU A 476 20.899 10.443 33.214 1.00 11.57	762 CD1 PHE A 473 18.379 11.788 41.031 1.00 14.53 763 CE1 PHE A 473 18.603 10.715 41.900 1.00 11.36 764 CZ PHE A 473 20.648 10.257 40.810 1.00 11.36 765 CE2 PHE A 473 20.648 11.329 39.954 1.00 13.01 767 C PHE A 473 20.444 11.329 39.954 1.00 13.01 768 O PHE A 473 20.044 11.329 39.954 1.00 13.01 769 N SER A 474 19.930 16.910 38.897 1.00 15.69 770 CB SER A 474 20.136 19.379 38.694 1.00 13.72 771 CB SER A 474 20.136 19.379 38.694 1.00 13.71 772 OG SER A 474 20.136 19.379 38.694 1.00 13.71 774 C SER A 474 20.136 19.379 38.694 1.00 13.47 775 C SER A 474 20.136 19.379 38.694 1.00 13.47 776 CB LYS A 475 20.878 17.435 35.597 1.00 13.49 777 CB LYS A 475 22.878 17.423 35.480 1.00 13.47 776 CJ LYS A 475 22.878 17.423 35.480 1.00 13.47 777 CB LYS A 475 22.878 17.423 35.480 1.00 12.47 778 CG LYS A 475 22.878 17.423 35.480 1.00 12.47 779 CD LYS A 475 22.878 17.204 35.033 1.00 13.73 780 CG LYS A 475 22.487 17.332 34.315 1.00 24.37 781 NZ LYS A 475 22.487 16.435 35.30 1.00 12.84 782 C LYS A 475 22.487 16.435 35.203 1.00 12.84 783 O LYS A 475 22.487 16.435 34.747 1.00 12.84 784 N LEU A 476 22.188 15.223 35.203 1.00 11.55 785 CB LEU A 476 21.567 16.436 34.747 1.00 12.84 786 CB LEU A 476 21.567 12.879 35.252 1.00 14.10 787 CG LYS A 475 22.487 16.436 34.747 1.00 12.84 788 CD LEU A 476 21.567 12.879 35.252 1.00 14.10 789 C LEU A 476 21.567 12.879 35.252 1.00 14.10 789 C LEU A 476 21.567 12.879 35.252 1.00 14.10 789 C LEU A 476 21.567 12.879 35.252 1.00 14.10 789 C LEU A 476 21.567 14.449 33.5.14 1.00 11.57	763 CE1 PHE A 473 18.603 10.715 41.900 1.00 11.36 764 CZ PHE A 473 19.726 9.961 41.785 1.00 8.01 765 CE2 PHE A 473 20.648 10.257 40.810 1.00 10.92 766 CD2 PHE A 473 20.648 10.257 40.810 1.00 13.01 768 O PHE A 473 19.944 11.329 39.954 1.00 15.68 769 N SER A 474 19.944 11.329 39.954 1.00 15.69 770 CA SER A 474 19.840 18.016 37.936 1.00 13.72 771 CB SER A 474 20.136 19.379 38.604 1.00 13.74 772 C SER A 474 20.702 17.877 36.691 1.00 13.44 774 O SER A 474 20.702 17.877 36.691 1.00 13.44 775 N LYS A 475 21.978 17.578 36.867 1.00 13.47 776 CA LYS A 475 22.878 17.435 35.754 1.00 13.47 777 CB LYS A 475 22.887 17.203 35.100 13.47 778 CG LYS A 475 22.888 17.204 35.031 1.00 13.47 779 CD LYS A 475 22.887 17.223 35.890 1.00 13.77 779 CD LYS A 475 22.887 17.243 35.891 1.00 13.77 779 CD LYS A 475 22.887 17.243 35.185 1.00 12.77 779 CD LYS A 475 22.887 17.243 35.185 1.00 12.77 779 CD LYS A 475 22.887 17.243 35.185 1.00 12.94 780 CE LYS A 475 22.467 16.436 34.747 1.00 12.94 781 NZ LYS A 475 22.467 16.436 34.747 1.00 12.94 782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 475 22.467 16.436 34.747 1.00 12.94 784 CG LEU A 476 21.832 14.124 34.294 1.00 11.68 785 CD LEU A 476 21.832 14.124 33.212 1.00 11.57 786 CB LEU A 476 21.832 14.124 33.212 1.00 11.57 787 CD LEU A 476 21.832 14.124 33.212 1.00 11.57 788 CD LEU A 476 21.832 14.124 33.212 1.00 11.57 789 CD LEU A 476 21.832 14.124 33.214 1.00 11.57 780 CD LEU A 476 21.832 14.124 33.214 1.00 11.57 780 CD LEU A 476 21.832 14.124 33.214 1.00 11.57 780 CD LEU A 476 21.832 14.124 33.214 1.00 11.57 780 CD LEU A 476 21.832 14.124 33.214 1.00 11.57 780 CD LEU A 476 21.832 14.124 33.214 1.00 11.57 780 CD LEU A 476 21.832 14.124 33.214 1.00 11.57 780 CD LEU A 476 21.832 14.124 33.214 1.00 11.57 781 CD LEU A 476 21.832 14.124 33.214 1.00 11.57 781 CD LEU A 476 21.832 14.144 33.214 1.00 11.57	764 CZ PHE A 473 19.726 9.961 41.785 1.00 8.01 765 CE2 PHE A 473 20.648 10.257 40.810 1.00 10.92 766 CD2 PHE A 473 20.644 11.329 39.954 1.00 13.01 767 C PHE A 473 19.944 15.623 38.527 1.00 15.68 769 N SER A 474 19.930 16.910 38.897 1.00 13.72 770 CA SER A 474 19.840 18.016 37.836 1.00 13.72 771 CB SER A 474 20.136 19.379 38.604 1.00 13.71 772 C SER A 474 20.136 19.379 38.604 1.00 13.44 774 O SER A 474 20.221 18.062 35.597 1.00 13.49 775 C SER A 475 20.221 18.062 35.597 1.00 13.49 776 CA LYS A 475 22.878 17.578 36.867 1.00 13.49 777 CB LYS A 475 22.878 17.435 35.784 1.00 13.47 778 CG LYS A 475 22.878 17.435 35.784 1.00 13.47 779 CB LYS A 475 22.878 17.435 35.784 1.00 13.47 779 CB LYS A 475 22.878 17.835 35.784 1.00 12.47 779 CB LYS A 475 22.878 17.835 34.315 1.00 13.47 779 CB LYS A 475 22.878 17.835 35.033 1.00 13.49 779 CB LYS A 475 22.878 17.835 35.033 1.00 13.47 779 CB LYS A 475 27.400 18.006 32.937 1.00 12.94 779 CB LYS A 475 22.467 16.436 34.347 1.00 12.94 780 CB LYS A 476 21.832 14.124 34.294 1.00 12.84 781 NZ LYS A 476 21.832 14.124 34.295 1.00 14.10 782 C LYS A 476 21.832 14.124 34.294 1.00 11.55 783 C LYS A 476 21.832 14.24 34.295 1.00 14.10 784 CB LEU A 476 21.832 14.24 34.294 1.00 11.55 785 CB LEU A 476 21.832 14.247 35.036 1.00 14.10 786 CB LEU A 476 21.832 14.247 35.036 1.00 14.10 787 CB LEU A 476 21.832 14.247 35.036 1.00 14.10 788 CD LEU A 476 21.832 14.449 35.280 1.00 11.55 791 C LEU A 476 20.899 10.456 33.289 1.00 11.56	765 CE2 PHE A 473 20.648 10.257 40.810 1.00 10.92 766 CD2 PHE A 473 20.444 11.329 39.954 1.00 15.05 767 C PHE A 473 20.018 15.623 38.527 1.00 15.69 768 N SER A 474 19.930 16.910 37.36 1.00 15.69 770 CA SER A 474 19.84 19.75 1.00 13.72 771 CB SER A 474 20.136 19.379 38.604 1.00 13.71 772 OG SER A 474 20.136 19.379 38.604 1.00 13.71 774 O SER A 474 20.136 19.379 38.604 1.00 13.73 775 CA SER A 475 20.702 17.877 36.691 1.00 13.44 776 CA LYS A 475 21.978 17.578 36.867 1.00 13.37 777 CB LYS A 475 22.88 17.578 36.867 1.00 13.37 778 CG LYS A 475 22.288 17.204 35.033 1.00 13.73 779 CB LYS A 475 22.288 17.204 35.033 1.00 13.73 779 CB LYS A 475 22.288 17.204 35.033 1.00 13.73 779 CB LYS A 475 22.288 17.204 35.033 1.00 13.73 780 CE LYS A 475 22.288 17.204 35.033 1.00 12.94 781 NZ LYS A 475 22.486 17.823 34.315 1.00 24.37 782 C LYS A 475 22.487 16.436 34.345 1.00 12.94 783 C LYS A 476 22.188 15.223 35.203 1.00 14.20 784 N LEU A 476 22.188 15.223 35.203 1.00 14.50 785 CB LEU A 476 21.892 10.287 35.056 1.00 14.10 786 CB LEU A 476 21.892 10.287 35.056 1.00 14.55 787 CG LEU A 476 21.892 10.287 35.050 1.00 14.83 788 CD LEU A 476 21.999 10.262 33.212 1.00 14.83 789 CD LEU A 476 20.897 10.4036 35.280 1.00 11.55 780 C LEU A 476 20.897 10.4036 35.280 1.00 11.55	766 CD2 PHE A 473	767 C PHE A 473 19.944 15.623 38.527 1.00 15.68 768 O PHE A 473 20.018 15.264 37.360 1.00 15.69 769 N SER A 474 19.830 16.910 38.897 1.00 13.72 770 CA SER A 474 19.840 18.016 37.936 1.00 13.11 771 CB SER A 474 20.702 17.877 36.691 1.00 13.44 772 C SER A 474 20.702 17.877 36.691 1.00 13.49 774 O SER A 474 20.702 17.877 36.691 1.00 13.49 775 CA LYS A 475 21.978 17.578 36.867 1.00 13.49 776 CA LYS A 475 22.878 17.274 10.01 2.47 777 CB LYS A 475 22.878 17.204 35.033 1.00 13.73 778 CG LYS A 475 22.878 17.204 35.033 1.00 13.73 779 CD LYS A 475 22.438 17.204 35.037 1.00 12.47 780 CE LYS A 475 22.438 16.736 33.530 1.00 14.20 781 NZ LYS A 476 22.438 16.736 33.530 1.00 12.84 782 C LYS A 476 22.438 16.736 33.530 1.00 12.84 783 C LYS A 476 22.188 15.223 35.203 1.00 12.84 784 N LEU A 476 22.188 15.223 35.203 1.00 12.87 785 CB LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.832 14.124 34.294 1.00 11.55 787 CG LYS A 476 21.832 14.124 34.294 1.00 11.57 788 CD2 LEU A 476 20.2879 11.262 33.512 1.00 14.83 790 C LEU A 476 20.899 11.262 33.512 1.00 14.83 791 C LEU A 476 20.599 11.262 33.528 1.00 14.83	768 O PHB A 473 20.018 15.264 37.360 1.00 15.69 769 N SER A 474 19.930 16.910 38.897 1.00 13.72 770 CA SER A 474 19.840 18.016 37.936 1.00 13.72 771 CB SER A 474 20.136 19.379 38.604 1.00 13.44 772 OG SER A 474 20.702 17.877 36.691 1.00 13.44 774 O SER A 474 20.702 17.877 36.691 1.00 13.49 775 N IVS A 475 22.878 17.579 1.00 13.49 776 CB IVS A 475 22.886 17.204 35.033 1.00 13.73 777 CB IVS A 475 22.886 17.204 35.033 1.00 12.47 778 CG IVS A 475 22.886 17.204 35.033 1.00 12.47 779 CD IVS A 475 22.467 16.436 34.315 1.00 24.37 779 CD IVS A 475 22.467 16.436 34.315 1.00 24.37 780 CE IVS A 475 22.467 16.436 34.215 1.00 24.37 781 NZ IVS A 475 22.467 16.436 34.215 1.00 12.94 782 C IVS A 476 22.438 16.736 33.530 1.00 14.20 784 N IBU A 476 22.188 15.223 35.203 1.00 12.84 785 CB IEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB IEU A 476 21.832 14.124 34.294 1.00 14.10 789 CD IEU A 476 21.999 11.262 1.00 14.10 789 CD IEU A 476 20.899 11.262 1.00 14.10 789 CD IEU A 476 20.899 11.262 33.212 1.00 14.10 789 CD IEU A 476 20.899 11.262 33.212 1.00 14.10 789 CD IEU A 476 20.899 11.262 33.212 1.00 14.10 789 CD IEU A 476 20.899 11.262 33.212 1.00 14.10	769 N SER A 474 19.930 16.910 38.897 1.00 13.72 770 CA SER A 474 19.840 18.016 37.936 1.00 13.11 771 CB SER A 474 20.136 19.379 38.604 1.00 14.23 772 OG SER A 474 20.136 19.379 38.604 1.00 14.23 773 C SER A 474 20.702 17.877 36.691 1.00 13.44 774 O SER A 475 20.221 18.062 35.597 1.00 13.49 775 CA LYS A 475 22.878 17.578 36.867 1.00 13.49 777 CB LYS A 475 22.878 17.208 36.867 1.00 12.47 778 CG LYS A 475 22.878 17.208 36.86 1.00 12.47 779 CD LYS A 475 22.878 17.208 36.85 1.00 12.47 779 CD LYS A 475 22.486 17.089 36.185 1.00 12.47 779 CD LYS A 475 22.486 17.204 35.033 1.00 13.73 780 CE LYS A 475 22.486 17.332 34.315 1.00 24.37 781 NZ LYS A 475 22.467 16.436 34.747 1.00 12.94 782 C LYS A 476 22.188 15.223 35.203 1.00 12.84 785 CA LEU A 476 22.188 15.223 35.203 1.00 12.84 786 CB LEU A 476 21.832 14.124 34.255 1.00 11.55 789 CD LEU A 476 21.832 14.124 34.255 1.00 11.55 789 CD LEU A 476 21.999 11.262 33.214 1.00 11.58 790 C LEU A 476 20.597 14.474 33.514 1.00 11.58	770 CB SER A 474 19.840 18.016 37.936 1.00 13.11 771 CB SER A 474 20.136 19.379 38.604 1.00 14.23 772 CG SER A 474 20.136 19.379 38.604 1.00 14.23 773 C SER A 474 20.702 17.877 36.691 1.00 13.44 774 O SER A 474 20.702 17.877 36.691 1.00 13.49 775 N LYS A 475 21.978 17.578 36.867 1.00 13.49 776 CA LYS A 475 22.878 17.635 35.754 1.00 12.47 777 CB LYS A 475 22.878 17.204 35.033 1.00 12.77 778 CG LYS A 475 22.878 17.204 35.033 1.00 12.77 779 CD LYS A 475 22.878 17.204 35.033 1.00 12.77 779 CD LYS A 475 22.467 16.463 35.185 1.00 24.37 779 C LYS A 475 22.467 16.436 34.747 1.00 12.94 781 NZ LYS A 475 22.467 16.436 34.747 1.00 12.94 782 C LYS A 475 22.188 15.223 35.203 1.00 12.94 783 O LYS A 476 22.188 15.223 35.203 1.00 12.94 786 CB LEU A 476 22.188 15.223 35.00 11.68 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 20.899 10.446 35.250 1.00 14.83 790 C LEU A 476 20.899 10.446 33.214 1.00 11.58	771 CB SER A 474 20.136 19.379 38.604 1.00 14.23 772 OG SER A 474 19.705 20.550 37.894 1.00 6.19 773 C SER A 474 20.702 17.877 36.691 1.00 13.44 774 O SER A 474 20.702 17.877 36.691 1.00 13.49 775 N LYS A 475 21.978 17.578 36.867 1.00 13.49 776 CA LYS A 475 22.878 17.435 35.754 1.00 13.37 777 CB LYS A 475 22.878 17.204 35.033 1.00 12.47 778 CG LYS A 475 25.288 17.204 35.033 1.00 12.77 779 CD LYS A 475 25.288 17.204 35.033 1.00 12.77 780 CE LYS A 475 25.288 17.204 35.033 1.00 13.73 781 NZ LYS A 475 27.400 18.006 32.937 1.00 24.37 782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 476 22.467 16.436 33.530 1.00 12.94 784 N LEU A 476 22.188 15.223 35.203 1.00 12.84 785 CR LEU A 476 21.832 14.24 34.255 1.00 14.10 786 CB LEU A 476 21.679 35.253 1.00 14.10 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.83 790 C LEU A 476 20.899 10.436 35.289 1.00 14.83 791 O LEU A 476 20.899 10.436 35.289 1.00 14.83	772 OG SER A 474 19.705 20.550 37.894 1.00 6.19 773 C SER A 474 20.702 17.877 36.691 1.00 13.44 774 O SER A 474 20.221 18.062 35.597 1.00 13.49 775 N LYS A 475 21.978 17.578 36.867 1.00 13.37 776 CA LYS A 475 22.878 17.435 35.754 1.00 12.47 777 CB LYS A 475 22.878 17.204 35.033 1.00 12.47 778 CG LYS A 475 22.878 17.204 35.033 1.00 12.77 779 CD LYS A 475 26.724 17.423 35.480 1.00 12.77 779 CD LYS A 475 26.724 17.423 35.480 1.00 12.94 780 CE LYS A 475 27.400 18.006 32.937 1.00 24.37 781 NZ LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 475 22.467 16.436 34.747 1.00 12.94 784 N LBU A 476 22.188 15.223 35.203 1.00 14.20 785 CA LBU A 476 21.832 14.124 34.294 1.00 11.58 787 CG LBU A 476 21.959 11.262 33.212 1.00 14.10 788 CD1 LBU A 476 20.899 10.436 35.250 1.00 14.83 790 C LBU A 476 20.899 10.436 35.250 1.00 14.83 791 O LBU A 476 20.608 14.449 33.514 1.00 11.58	773 C SER A 474 20.702 17.877 36.691 1.00 13.44 774 O SER A 474 20.221 18.062 35.597 1.00 13.49 775 N LYS A 475 21.978 17.578 36.867 1.00 13.49 776 CA LYS A 475 22.878 17.435 35.754 1.00 12.47 777 CB LYS A 475 22.878 17.204 35.033 1.00 12.47 777 CB LYS A 475 25.288 17.204 35.033 1.00 12.77 778 CG LYS A 475 26.724 17.423 35.480 1.00 12.77 779 CD LYS A 475 26.724 17.423 35.480 1.00 12.77 780 CE LYS A 475 27.400 18.006 32.937 1.00 24.37 781 NZ LYS A 475 27.400 18.006 32.937 1.00 24.37 782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 476 22.487 16.736 33.530 1.00 14.20 784 N LEU A 476 22.188 15.223 35.203 1.00 12.84 785 CA LEU A 476 21.872 14.124 34.294 1.00 11.55 787 CG LEU A 476 21.672 11.659 34.255 1.00 14.10 788 CD1 LEU A 476 21.999 11.262 33.212 1.00 14.10 789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.899 10.436 32.289 1.00 11.58	774 O SER A 474 20.221 18.062 35.597 1.00 13.49 775 N LYS A 475 21.978 17.578 36.867 1.00 13.37 776 CA LYS A 475 22.878 17.435 35.754 1.00 12.47 777 CB LYS A 475 22.878 17.435 35.754 1.00 12.47 778 CG LYS A 475 25.288 17.204 35.033 1.00 12.77 779 CD LYS A 475 26.724 17.423 35.480 1.00 13.73 779 CD LYS A 475 27.440 18.006 32.937 1.00 24.37 781 NZ LYS A 475 27.460 18.006 32.937 1.00 24.37 782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 476 22.488 15.223 35.203 1.00 14.20 784 N LEU A 476 21.867 12.879 35.056 1.00 14.20 785 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.099 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 20.899 11.262 33.212 1.00 14.83 790 C LEU A 476 20.899 10.436 35.250 1.00 14.83 791 O LEU A 476 20.597 14.474 33.514 1.00 11.58	775 N LYS A 475 21.978 17.578 36.867 1.00 13.37 776 CA LYS A 475 22.878 17.435 35.754 1.00 12.47 777 CB LYS A 475 22.878 17.435 35.754 1.00 12.47 778 CG LYS A 475 25.288 17.204 35.033 1.00 12.77 779 CD LYS A 475 26.724 17.423 35.480 1.00 13.73 779 CD LYS A 475 26.724 17.423 35.480 1.00 16.66 780 CE LYS A 475 27.742 17.332 34.315 1.00 24.37 781 NZ LYS A 475 27.740 18.006 32.937 1.00 24.37 782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 475 22.467 16.436 34.747 1.00 12.94 784 N LEU A 476 22.188 15.223 35.203 1.00 14.20 785 CB LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 14.10 789 CD2 LEU A 476 21.999 11.262 33.212 1.00 14.10 789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.698 14.474 33.514 1.00 11.58	776 CA LYS A 475 22.878 17.435 35.754 1.00 12.47 777 CB LYS A 475 24.286 17.089 36.185 1.00 12.77 778 CG LYS A 475 25.288 17.204 35.033 1.00 12.77 779 CD LYS A 475 26.724 17.423 35.480 1.00 13.73 779 CD LYS A 475 27.742 17.332 34.315 1.00 24.37 781 NZ LYS A 475 27.742 17.332 34.315 1.00 24.37 782 C LYS A 475 27.460 18.006 32.937 1.00 24.37 783 O LYS A 475 22.467 16.436 34.747 1.00 12.94 784 N LEU A 476 22.188 15.223 35.203 1.00 14.20 785 CA LEU A 476 22.188 15.223 35.203 1.00 12.84 786 CB LEU A 476 21.832 14.124 34.294 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 21.999 11.262 33.212 1.00 14.10 789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEÜ A 476 20.899 10.436 35.289 1.00 11.58	777 CB LYS A 475 24.286 17.089 36.185 1.00 12.77 778 CG LYS A 475 25.288 17.204 35.033 1.00 13.73 779 CD LYS A 475 26.724 17.423 35.480 1.00 13.73 780 CE LYS A 475 27.742 17.332 34.315 1.00 24.37 781 NZ LYS A 475 27.742 17.332 34.315 1.00 24.37 782 C LYS A 475 27.400 18.006 32.937 1.00 24.37 783 O LYS A 475 22.467 16.436 34.747 1.00 12.94 784 N LEU A 476 22.188 15.223 35.203 1.00 12.84 785 CA LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEÜ A 476 20.899 10.436 35.289 1.00 11.58	778 CG LYS A 475 25.288 17.204 35.033 1.00 13.73 779 CD LYS A 475 26.724 17.423 35.480 1.00 16.66 780 CE LYS A 475 27.742 17.332 34.315 1.00 24.37 781 NZ LYS A 475 27.400 18.006 32.937 1.00 24.37 782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 475 22.438 16.736 33.530 1.00 14.20 784 N LEU A 476 22.188 15.223 35.203 1.00 12.84 785 CA LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.899 10.436 35.250 1.00 14.83 791 O LEU A 476 20.597 14.474 33.514 1.00 11.58	779 CD LYS A 475 26.724 17.423 35.480 1.00 16.66 780 CE LYS A 475 27.742 17.332 34.315 1.00 24.37 781 NZ LYS A 475 27.400 18.006 32.937 1.00 24.37 782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 476 22.488 16.736 33.530 1.00 14.20 784 N LEU A 476 22.188 15.223 35.203 1.00 12.84 785 CA LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 21.999 11.262 33.212 1.00 14.10 789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEÜ A 476 20.597 14.474 33.514 1.00 11.58	780 CE LYS A 475 27.742 17.332 34.315 1.00 24.37 781 NZ LYS A 475 27.460 18.006 32.937 1.00 23.53 782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 475 22.438 16.736 33.530 1.00 14.20 784 N LEU A 476 22.188 15.223 35.203 1.00 14.20 785 CA LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 21.999 11.262 33.212 1.00 14.10 789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEÜ A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.597 14.474 33.518 1.00 11.58	781 NZ LYS A 475 27.400 18.006 32.937 1.00 23.53 782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 475 22.467 16.436 34.747 1.00 12.94 784 N LEU A 476 22.188 15.223 35.203 1.00 14.20 785 CA LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.597 14.474 33.518 1.00 11.58	782 C LYS A 475 22.467 16.436 34.747 1.00 12.94 783 O LYS A 475 22.438 16.736 33.530 1.00 14.20 784 N LEU A 476 22.188 15.223 35.203 1.00 14.20 785 CA LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.597 14.474 33.518 1.00 11.58	783 O LYS A 475 22.438 16.736 33.530 1.00 14.20 784 N LEU A 476 22.188 15.223 35.203 1.00 12.84 785 CA LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.597 14.474 33.518 1.00 11.58	784 N LEU A 476 22.188 15.223 35.203 1.00 12.84 785 CA LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.608 14.449 32.289 1.00 11.58	785 CA LEU A 476 21.832 14.124 34.294 1.00 11.68 786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.999 11.262 33.212 1.00 14.10 788 CD1 LEU A 476 21.999 11.262 33.212 1.00 12.17 789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.608 14.449 32.289 1.00 11.58	786 CB LEU A 476 21.567 12.879 35.056 1.00 11.55 787 CG LEU A 476 21.072 11.659 34.255 1.00 14.10 788 CD1 LEU A 476 21.999 11.262 33.212 1.00 12.17 789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.608 14.449 32.289 1.00 11.58	787 CG LEU A 476 21.072 11.659 34.255 1.00 14.10 788 CD1 LEU A 476 21.999 11.262 33.212 1.00 12.17 789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.608 14.449 32.289 1.00 11.58	788 CD1 LEU A 476 21.999 11.262 33.212 1.00 12.17 789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.608 14.449 32.289 1.00 11.58	789 CD2 LEU A 476 20.899 10.436 35.250 1.00 14.83 790 C LEU A 476 20.597 14.474 33.514 1.00 11.27 791 O LEU A 476 20.608 14.449 32.289 1.00 11.58	790 C LEU A 476 20.597 14.474 33.514 1.00 11.27	791 O LEU A 476 20.608 14.449 32.289 1.00 11.58	

																														•											
D	Ċ	ບ	ບ	ပ	U	0	Z	ပ	ບ	ບ	0	Z	ပ	0	Z	ບ	U	Ü	0	0	ບ	0	z	Ü	Ö	Ö	0	Z	ບ	0	z	υ	ບ	ບ	ט	ບ	Ü	0	×	Ui-	ບ
																																	•								
										-	-																														
27	53	22	69	8	03	74	35	17	15	45	20	00	46	14	99	55	69	13	57	87	54	94	80	52	25	64	62	94	85	00	91	95	62	74	82	84	93	37	.61	96	95
7	6	ø.	'n	ď	Ġ.	Ŋ.	4	ø.	'n.	Ŋ.	Ġ	ď	ŵ	ø.	υ.	7.	7.	4	8	H	7.	ω.	ė.	Ŋ.	4.	57	ω.	ις.	4	8	ď.	Ġ.		ω.	7		٠	00	'n	4	
_	0	0	_	_	_	_	_	_	_	_	_	_																													•
õ	8	9	00	00	8		8	8	00	00	8	00	8	00.	0	0	0	00	00.	00.	8	8	90.	00	90.	00.	00.	8	00.	00	8	8	90.	8	00	0	00	0	00	00	00
-	H	H	Ä	H	નં	H	નં	H	નં	H	Η̈́.	નં	નં	H	H	H	H	Η̈́.	ΐ	H	ä	H	H	ਜਂ	H	ä	ä	તં	ä	÷.	i,		\ddot{H}	ä	$\ddot{-}$	ä	ä	ä	ä	ä	i
~	4	0	m	7	낸	c#	₩.	7	σ.	σ	m	ო	7	0	Н	_	10	10	_		10	10	~		_	_	~	_	•	_		_	_						_	_	
63	724	43	53	36.	9	16,	78	87	53	ij	96	77	26	68	.9	36	75	.706	걾	986	146	165	.063	34.1	9	34(188	620	33	348			.829						179	H	2
•	4	•	36.	•	•	•	•	•	•	•	•	•	•	•	•	9			-:	8	.:		7.		-		7.	~ ~				-	~;	~	2.	-		<u>:</u>	ις ω:	7.7	.2
~	m	m	ന	m	m	M	m	W	32	m	m	'n	m	29	m	N	N	N	27	N	Ñ	7	7	7	ñ	7	22.48	7	7	7	7	ñ	7	7	2	7	7	2	2		2
C	9	4	Ŋ	œ	0	02	o	0	'n	_	9	4	2	7	œ	9	ო	4																						Ŋ	7
2	25.1	93	10	8	N	æ	31	47	78	397	84	374	25	12	60	766	64	34	08	31	30	23	.062	76	83	630	413	7.638	35	55	05	72	604	69	42	26	260	55	999	59	9
r.	15	m	4	7	ė,	Ġ	7	œ.	ď	ö								'n.	'n	'n	6	īυ.	7	é	~	6		7.	ņ.	4.	15.	е Э	ω.	4.	4	ď	7	•	•		•
•			1-1		_	П	_		_	CA	N	(1	П		171									Н	Н	Н	Н	Н	7	m	Н	Н	Н	Н	Н	H	Н	Н	-	Н	Н
7	1 1	00	11	67	36	34	33	54	16	12	15	45	24	37	2	72	0	9	90	4.708	7	5	33	8	9	2	6	m	7	N	7	ᅼ	2	0	æ	ក	ų	4		ø	4
S	Ŋ	ō.	œ	Ğ.	. 23	7	28	7	.71	.61	.61	7.	.05	.03	7	.572	ķ	ij	ĕ	5	7	7	.893	<u> </u>	2	7.	.369	.46	.52	.63	.81	.28	.805	.48	.20	.20	71	36	65	0	9
α	17	17	15	ဖ	œ	17	13		13	œ	17	18	0	20	0	27	22	23	23	24	20	20	20	20	20	5	0	8	0	9	ቪ	2	<u>ب</u>	4.	4.	4.	Ξ.	넊	21.	ᆏ	
												-	•	•		•	•	•	•	•	•••	•	•	•	•	•••	• •	• •	•	• •	•	.,	.,	•••	.,	.,	.,	"	.,	W.	"
_	_	_	_	_		_										_	_	_		_																					
2	477	4,77	477	177	177	77	78	178	478	78	78	478	78	78	7.9	7.9	79	479	79	79	79	79	80	80	80	80	480	80	80	80	81	81	481	81	81	481	481	81	82	482	82
	. 4:			A	4	4	4	4	4	4	4	4	4	A 4	A																			4							4
		•	•		J 7	3 7	7	7	Z4	7	17	•	24		-	•	<	•	A.	4	4		¥		A	-	A	Z -	A	A	4	Ø	4	4		•	4	Ø	Ø	⋖	•
Ē		曾	Ħ	널	LEU	Ħ	ASN	ASN	S	ASN	ASN	ASN	ASN	ASN	SI	SI	SE	ASP	SE	SE	SE	SE	ASN	S	SI	S	ASN	ASN	ASN	SN	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	田	PHE	PHE
								-																																	
5	5 8	ည	ä	Ä	7)	0	5	S	g	ង	Ä	ĕ	<i>r</i>)	_	<u>ج</u> ا	K	Ą	ង	ĕ	ă	r s	_	ь	Ą	m	ថ្ក	Ë	92	. .	_		ď	Ą	5	ᄗ	Ğ		_	_	4	മ
											J	~		Ü	4	•	J	Ü	U	V	0	U	4	U	U	U	O	14	J	O	4	U	O	O	O	O	O	O	z	O	Ö
ç	794	95	96	97	98	99	00	7	2	803	4	5	90	7	8	60	2	디	2	2	4	പ	9	5	80	9	820	821	Ŋ	ŭ	4	ល	9	2	œ	Ø.	0	ᅼ	Ŋ	m	
7		7	-	-	7	-	œ	œ	œ	œ	œ	ω	æ	œ	ω̈	æ	80	œ	œ	œ	œ	œ	œ	ω.	œ	8	8	œ	8	8	8	8	82	8	82	8	8	8	83	83	83
2	Ξ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	Σ	>	>	>:	7	7	7	5	7	7	~	>	5	5	⋝ '	7	5	5	~	V
E	ATOM	2	ATOM	5 F	ATOM	T _O	ATOM	Į,	ATOM	ĮŎ.	ATOM	Ę,	Ď	ATOM	ATOM	Ę,	Q	ATOM	ATOM	<u>S</u>	뎓	ATOM	ATOM	ATOM	ğ	ATOM	ATOM	ATOM	ATOM	ATOM	õ	ATOM	ATOM	ű	ATOM	ATOM	ATOM	ğ	ATOM	ATOM	ATOM
~	ς α	K	ď	ď	ď,	Z,	K	A	K	ø	Æ	K	Ø	4	d	ø	A	A	ď	Þ	ď	ď	Þ	Þ	Ø,	A	ø	A	Þ	Þ	A	A	Þ	Ā	A	Æ	A	A	A	A	A.

20000002000000000000000000000000000000	U
2	4.
	1.00
00111077770000000044001111000040404007	23.690
ορισιομομομομοισισισισισισισισισισισισισισ	7.731
	4.
E E E E E E E E E E E E E E E E E E E	4
CG PHE CD1 PHE CC2 PHE CC2 PHE CC2 PHE CC2 PHE CC2 PHE CC3 PHE CC4 PHE CC5 PHE CC6 HIS CC6 HIS CC6 HIS CC7 PHE) IEC
835 GG 836 GD1 837 GE1 838 GZ 845 GD2 845 GG 845 GB 845 GB 845 GB 845 GB 855 GG 855 GG	376 CJ
	ATOM 8

ט ט	ე.	บ	ບ	0	z	ບ	ບ	บ	0	Z	บ	บ	ß	ບ	Ο.	Z	U	υ	ပ	0	Z	ט	ບ	υ	ບ	ບ	ပ	0	z	ບ	ບ	ບ	บ	0	0	ບ	0	Þ	ပ	Ω.
4.14 86	9	٥.	3.80	0	Ċ		9	4	٥.	٦.	5.29	ü	5.78	5.44	4.75	5.61	5.43	6.08	4.62	2.60	3.23	2.52	2.72	2.48	5.00	2.00	3.77	3.11	5.20	7.70	7.57	0.36	2.45	ű	ø.	'n	•	4	0	55
1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00		1.00				1.00	00.	1.00	00.		1.00	.00	00.	00.	1.00	00.	00.	1.00			1.00 1	.00 1	.00	.00	00.	00.	.00	1.00 10	.00
23.196	• •	2.75	22.477	2.19	1.83	20.698	0.27	.09	ö	.19	N	23.837	24.279	22.729	•	•			22.406				•		•	19.324		4.	19.522	. 74	.90	18.193	. 73	16.081	16.213	19.162	18.346	20.445	0.9	22.536
9.150	7.		6.785	.90	•	•	6.594	4.758	3.885	•	•	•	•	•	•	3.233	2.829	3.780	2.669	1.779	3.472	3.330	4.622	5.885	7.153	5.660					86	•	7	•	.46	-0.480	-1.384	-0.597	0	. 7
14.104	.50	. 65	4.7	3.88	5.87	6.29	7.69	.34	5.80	6.99	7.12	9	8.23	5.73	15.444	•	13.503	•	12.700	•	•	8	•	•	•	ö	ĸ.	•	14.109	•	•	16.964	16.581	. 43	.433	14.102	.91	13.806	.230	13.208
87	87	487	487	487	88	488	88	488	488	489	489	89	489	89	489	90	90	90	490	90	91	491	91	491	91	491	91	491	492	92	92	492	492	92	92	492	32	93	193	. 26
LEU A 4	LEU A 4	LEU A 4	¥	4	ø	Ø	ď	ď	ø	ø	ď	ø	ø	ø	CYS A 4	4	ø	ď	ALA A 4	ALA A 4	LEU A 4	ø	ď	ø	LEU A 4	ď	ď	LEU A 4	æ	ø	Þ	GLU A 49		GLU A 49		GLU A 49	GLU A 49	A A	A 4	VAL A 45
8 8	9 6	CD2	ບ	0	×	ජ	G	ບ	0	×	ð	පු	SG	ບ	0																	_	_	_	-	_	0	z	CA C	9
877	879	880	881	œ	æ	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	606	910	911	912	913	914	915	916	917	918
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

									•													•														-			
																																	•						
8.23	η. Ψ	10.6	0.1	Ψ.	ι.	6.4	2.	2.6	ო ო	Ġ	4.6	ы 2	 	Η.	6.4	5.6	8.7	7.7		3.0	2.0	Q	6.	7.3	9.4	5.1	4.	0.0	3.4	6.8	6.2	7.4	Ė		0		5.9	35.68	9.1
1.00	80.	0	۰.	۰.	٥.	۰.	۰.	0.	0	0	٥.	0	0	°.	0	۰.	۰.	۰.	0	0	0	1.00	1.00	٥.	1.00	0		•	٥.	•	0	0	•		°.			1.00	1.00
3.12		0.43	0.0	0.2	9.61	1.85	8.56	8.17	7.74	.32	5.53	5.54	4.53	2.89	5.99	.93	.88	6.68	7.75	.77	5.92	17.836	8.00	. 22	Ø	0.36	œ	6.45	6.10	4.92	4.98	6.32	. 75	8.01	2	.07		17.183	LO
. e.	യസ	0.92	8	.33	.32	. 54	Ø	.21	. 72	1.03	.03	.31	.32	S	43	96.	9	.31	9	4	9	-5.221	2	4	7	.59	ų.	. 44	ä	.20	•	-3.904		.69	9	3.4	-2.731	-2.865	.24
17 60	8.4	.01	.63	8	.53	55	.55	. 75	0.36	34	1.09	0.40	1.31	Н	0.87	0.58	1.68	2.29	.31	1.21	1.09		.43	. 65	.87	.60	8.512	.06	.25	.36	.36	.69	.75	.16	. 52	.97	4.	0	.07
493 493		י סי		494	494			494	495	495	495	495	495	495	495	495	g	Ō	496	496	496	497	497	497	497	497	497	497	498	498	498	498	498	ð	498	498	498	498	o,
VAL A	VAL A	VAL A	•		•	•	•	-	-	MET A	-	•	-	•	-	-	ALA A		ALA A	•	•	THR A		•	THR A		THR A	•	•	TYR A	TYR A		TYR A	•		TYR A	TYR A	TYR A	TYR A
CG1 CG2	ပင) Z	ජ	ස	CG1	CG2	ບ	0	×	ජ	ස	සු	SD	Œ	ບ	0	z	Ð	8	ບ	0	×	đ	8	061	CG2	ບ	0	z	ස	ස	පු	9	CE1	ZZ	НО	CE2	CDS	U
919	921	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	926	957	958	959	960
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

50.50 52.41 52.41 69.40 69.92 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60.90 60 45.09 46.76 48.01 47.71 12.338 12.951 11.084 9.973 11.378 10.409 10.797 9.631 10.020 10.043 9.976 10.132 10.321 10.489 10.092 9.992 11.026 10.893 8.587 7.983 0.420 0.420 0.559 0.499 1.851 2.552 0.436 2.179 -4.693 -5.887 -5.935 -6.704 -5.924 -5.927 -10.619 -10.547 -10.961 -10.052 -7.563 -8.292 -10.619 -10.547 -10.961 -10.547 -10.961 -7.563 -8.171 -6.248 -6.248 -5.356 -4.738 -4.752 1.112 0.166 -1.239 -1.704 0.689 -0.084 2.013 2.644 2.435 3.403 1.160 0.527 7.561 9.233 9.962 11.290 12.305 9.098 9.103 8.382 7.476 7.233 6.773 6.773 5.473 6.124 5.050 6.211 5.058 5.166 4.924 3.844 9.297 10.177 10.072 8.726 11.636 11.733 13.075 14.026 2.045 16.036 14.498 SER A A SER A A ARG A AR

																																		•							
ન ા •	ۍ د د		o. 1	۳. ا	ດ '	2.6		7.1	8.	ø.	ø.	9.	4.8		2.3	9.7	0.7	4.0	6.4	5.2	3.0	9.6	17.88	3.5	7.78	7.6	ø.	5.65	7.37	e o	21.97	Ø	w	3.7	3.7	9	근.	ij	•	6.57	•
1.00	.		1.00	0	0	0	0		0	0		00	00	00	00		00	1.00	00	1.00	00	00		00	1.00	00	1.00	1.00	00	00	00	00	O	00	00	00	00	1.00	0	1.00	1.00
6.998	. 44	82.	90.	9.743	8.093	7.827	9.322	10.492	11.720	13.093	13.429	13.278	10.273	o	4-4	11.342	9.931	9.250	12.154	11.624	13.460	14.402	14.932	15.659	15.466	16.127	17.011	17.219	16.539	13.883	41	.07	.67	.61	•	12.404	.18	49	ū	10.997	4
1.400	1.024	1.485	2.709	0.693	1.018	0.716	1.009	0.764	0.548	0.486	.0.968	1.573	-0.390	1.031	.0.607	.1.586	.1.943	.2.859	-0.743	0.031	.0.922	-0.177	-0.914	-0.038	.0.135	0.675	1.632	1.743	0.919	1.160	2.200	1.189	2.461	2.056	0.796	0.062	.49	4.693	۰.	4.084	٣.
•	2.05	1.75	11.716	.55	4.4	5.6	13.953	4.79	m	4	ß	5.676	5.743	5.760	6.542	7.599	8.113	7.245	8.597	9	ω.	9.332	0.495	1.410	ς.	ന	ω.	ij	0	ď	o.	ö.	ä	ď	2.04	1.58	0.44	છ	9.35	œ	7.11
511	511	511	511	511	511	511	512	512	512	512	512	512	512	512	513	513	513	513	513	513	514	514	514	514	514	514	514	514	514	514	514	515	515	515	515	515	515	515	516	516	516
ASP A	ASP A	ASP A	ASP A	ASP A		ASP A	Ø	ø	ď	Ø	Ø	Æ	Ø		ø	ø	ø		ø	ø	ø	Ø	Ø	ø	¥	4	¥	ø	ø	ø	ø		ø	ø	æ	_	Ø	ø	ď	ø	TRP A
r S	ප	ង	001	OD2	ט	0	z	đ	CB	ຕູ	907	CD5	ซ	0	Z	G	9	90	່ບ	0	Z	ð	8	b	CDT	CET	CZ	CE2	9	ບ	0	z	ð	8	8	ė	ບ	0	×	G	9
1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1013	1014	1015	1016	1017	1018	1019	1020	1021	1022	1023	1024	1025	1026	1027	1028	1029	1030	1031	1032	1033	1034	1035	1036	1037	1038	1039	1040	1041	1042	1043	1044
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

OCZO	טטטט	CCOZ		ט בא סט פ	0 0 0 0 0	OSUUUC) X U O X U U U O
8000	8888	00000			00000		00 22.67 00 10.46 00 11.31 00 9.13 00 10.43 00 10.55 00 13.73 00 6.90
797 538 286 354	10.333 11.555 11.741 10.761	9.569 1 12.003 1 11.702 1 13.200 1	15.545 16.492 15.859	14.585 14.379 14.739	14.639 15.627 15.647 16.977 13.817	10.25.11 11.52.11 11.52.11 10.162 10.094	8.169 11.701 11.701 11.701 11.879 12.095 12.461 11.201 13.191 13.091
					. W , 11 11 11 11 11 11 11 11 11 11 11 11 1	•	
16.106 16.196 15.058 14.229	14.860 14.213 12.976 12.376	13.015 17.952 17.926 17.666	17.185 16.858 15.951 14.834	18.212 17.848 19.497 20.514	21.899 22.196 23.684 21.682	20.237 20.237 20.409 20.366 20.446 21.098	20.268 19.046 19.004 17.949 16.709 15.620 14.333 15.317 16.771
TRP A TRP A TRP A	TRP A 5 TRP A 5 TRP A 5	TRP	ILE A A ILE A A ILE A A A E E E E E E E E E E E E E E E E	ILE A ILE A LEU A	LEU A LEU A LEU A		ASN A ASN A ASN A ASN A VAL A
1045 CG 1046 CD1 1047 NE1 1048 CE2		1053 CZZ 1054 C 1055 O				1071 O 1072 N 1073 CA 1074 CB 1075 CG	
ATOM ATOM ATOM			ATOM ATOM ATOM ATOM I				•

•																																										
																																						_				
	5.11	س	ų.	•	ო.	?	۰.	ď	2.73	2.77	3.11.	2.00	5.97	2.15	2.00	3.48	2.26	3.51	5.69	3.52	3.71	12.53	3.88	4.01	2.74	2.84	2.00	2.00	2.78	7.61	11.33	3.34		4	_	5.69	4	Ŋ	2.00	Ч	5.32	6.17
	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	14.314	4.	۲.	16.854	.17	16.779	15.474	16.394	14.458	14.488	14.324	13.874	13.307	13.998	15.773	16.287	16.200	17.427	18.177	19.629	19.873	19.828	17.090	16.297	17.716	17.474	17.836	17.147	15.679	14.980	13.479	18.109		•	•		•	20.264	•	20.806	20.777	22.059
	10.792	. 71	.94	Ξ.	.28	8	12.577	13.401	12.407	13.075	14.599	15.287	14.661	16.571	12.71	13.624	11.539	11.082	10.220	9.986	8.528	9.957	10.191	9.219	10.461	9.601	10.334	11.724	.58	12.949	12.847	8.202	7.964	7.261	5.910	5.015	5.816	5.010	6.610	6.484	7.286	0
	17.443	17.522	17.357	16.071	15.983	14.901	18.823	19.011	19.688	20.955	20.752	21.989	22.890	22.010	21.802	22.511	21.783	22.438	21.428	21.532	20.849	22.971	23.614	23.485	24.746	25.903	27.149	27.149	-	27.418	1-	41	ш	w	26.598	27.316	27.273	w	28.325	29.027	30.353	П
		Ø	LEU A	ASN A	ASN A	ASN	ASN A	LEU A	LYS A 524	LYS A	LYS A	LYS A	ALA A	ALA A	ALA A	ALA A	ALA A		PHE A	PHE A 526	PHE A 526																					
	×	_									9																											0	Z	ర్	CB	ပ္ပ
	1087	1088	1089	1090	1091	1092	1093	1094	1095	1096	1097	1098	1099	1100	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112	1113	1114	1115	1116	1117	1118	1119	1120	1121	1122	1123	1124	1125	1126	1127	1128
	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM																													

υυυυ	יבסטט	υυυοο	טטאטט	טטטט	υυςουυυ	000000	ひひひはひひひ
	ஒ வ வ வ	4 4 18 2 2 0 0 2 3 4 4 8 3 5 6 9 5 6 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	4.67 6.22 4.38 7.25		• • • • • •	<u> </u>	8.73 7.03 6.96 7.01 7.93 8.59
0000	\circ		1.00	1111			1.00 0.00 0.00 0.00 0.00
22.377 23.581 24.568	23.014 21.983 23.098 21.773	22.846 22.496 22.359 23.205 21.454	23.150 24.286 22.136 22.227 20.803	20.713 20.311 20.164 20.441	20.784 20.917 23.126 24.084 22.816 23.562	24.090 24.986 26.088 26.287 27.345 25.405	24.312 25.069 25.848 25.478 26.893 27.075
6.036 5.936 7.010 8.187	8.274 6.884 6.292 7.911			4.250 4.782 3.975 2.577			3.849 3.312 2.457 4.532 4.848 6.323 6.736
31.814 32.505 32.494 31.822	31.111 28.109 28.240 27.251	26.313 25.701 26.718 27.665 26.598	25.187 24.739 24.737 23.658 23.358	22.132. 20.924 19.799	21.068 22.218 24.105 23.425 25.289 25.938	28.385 28.491 29.389 30.151 31.044	29.151 25.935 25.690 26.238 26.239 27.919
PHE A 526 PHE A 526 PHE A 526 PHE A 526	**		**	**	PHE A 528 PHE A 528 PHE A 528 PHE A 528 TYR A 529 TYR A 529	A A A B S S S A A A A B S S S A A A B S S S A A A B S S S A A B S S S S	TYR A 529 TYR A 529 TYR A 529 LYS A 530 LYS A 530 LYS A 530 LYS A 530
G G G G G G G G G G G G G G G G G G G	NO C B	66 G G G G G G G G G G G G G G G G G G	00200	6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	B G × 0 0 G G	GE 11 GE 12 GE 13 GE 14	G G F F O C G
1129 1130 1131 1132	1133 1134 1135 1136	1137 1138 1139 1140 1141	1142 1143 1144 1145	1148	1151 1152 1153 1154 1155 1155	1158 1159 1160 1161 1162 1163	1165 1165 1166 1167 1168 1169
ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM

•

6.67 6.39 6.39 6.39 111.11 116.80 19.44 19.44 6.18 6.18 6.18 4.84 4.32 4.45 5.96 5.10 1.00 1.000 00.1 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 26.381 27.787 27.510 28.299 24.083 22.877 28.285 28.507 29.691 30.317 31.320 31.725 32.935 30.776 31.395 30.998 32.030 25.387 27.837 30.800 32.279 31.664 32.781 -0.133 -1.674 -1.055 -1.055 -1.055 -2.671 -2.996 -1.098 -1.098 -1.098 -1.098 -1.098 -1.066 1.762 2.236 -0.250 2.400 0.034 0.055 0.244 0.649 0.649 0.411 2.187 28.593 27.983 24.983 24.983 24.983 22.983 21.123 22.123 22.123 22.429 23.696 22.953 23.696 23.696 23.677 22.953 23.696 23.677 23.696 23.696 23.677 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 23.696 TLE TLE GLU GLU GLU GLU GLU GLU GLU SER SER SER SER SER PHE PHE GLU VAL ILE ILE ILE VAL APT. GLU 1174 1175 1176 1177 1178 1179 1180 1181 1182 1183 1184 1185 1186 1187 1188 1189 1190 1191 1192 1193 1194 1195 1196 1197 1198 1199 1200 1201 1202 1203 1204 1205 206 1208 1207

 σ

טט	ט	•	Z	ບ	ບ	ບ	U	U	ບ	0	Z	Ö	ບ	ບ	Ö	ບ	Z	ပ	0	Z	ບ	ပ	ບ	0	×	ບ	ບ	ບ	ບ	0	0	ບ	0	Z	ບ	ບ	0	×	U	ن
7.49	ι.		H.	•	•	2.00	•	2.46	6.22	7.20	7.13	7.81	8.38	1.82	0.54	6.43	6.23	6.91	7.82	6.92	5.49	4.12	6.38	6.33	7.70	8.69	0	0.13	•	•	1.46	æ	1.40	8.74	•	8.50	ī.	•	6	
1.00	1.00	1.00		1.00		1.00	1.00	1.00	1.00	1.00	1.00	1.00	0			1.00 2			00.		00.		00.			1.00	1.00 1	00.	1.00 1	1.00 1	Н		Н			0		0	0	00
26.907	0.16	0.62	9.89	0.16	9.67	8.16	27.637	0.16	ä	1.91	32.571	4.01	4.92	4.63	5.58	5.15	6.31	4.54	Ŋ.	•	.37	ω.	3.96	4	Ö	32.354	8.0	ö	ä	31.629	.74	2.55	•	•	33.832	2.88	ď	è	31.125	31.090
1.683	18	1.47	-2.093	.49	-4.347	-4.414	-4.726	•	-3.836	-4.791	-3.082	-3.360	-2.954	('1	-2.777	-2.945	-2.886	α	-3.015	-1.626	-0.901	0.503	-1.537	-1.305	-2.296	•	•	.03	-2.643	•	-3.560	.37	-5.145	-4.820	-6.240	-7.044	-8.249	.41	-7.177	
15.156	8.1	7.05	σ	8.87	ö	0.01	급	•	•	•	19.245	19.039	20.210	21.589	22.582	24.072	25.029	17.853	17.360	17.402	16.250		14.926	•	•	•	•	12.180	11.089	10.984	10.377	3.6	14.241	12.982	12.926	2.0	٥.	11.296	10.420	9.033
PHE A 535	A		Ø	Ø		ø	ď	ø	K	ILE A 536		Ą		æ		Ø	ď	K	ø	Ø			ALA A 538	ď	ø			ø	4	ď	A 53	A 53	GLU A 539	4	GLY A 540	വ	4	54	ASN A 541	54
CE2	່ວ	0	z	ð	GB	CG1	CDI	CG2	ບ	0	z	đ	CB	ဥ	9	CE	NZ	ບ	0	×	ජ	සු	ບ	0	z	ð	CB	ຶ່ນ	8	OE1	OE2	ບ	0	z	g	ບ	0	z	g	g
1213	1215	1216	1217	1218	1219	1220	1221	1222	1223	1224	1225	1226	1227	1228	1229	1230	1231	1232	1233	1234	1235	1236	1237	1238	1239	1240	1241	1242	1243	1244	1245	1246	1247	1248	1249	1250	1251	1252	1253	1254
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

2.8	ų.	4	ė.	٠.		ተ '	9 (٠.	Φ.	ന	4	<u> </u>	ω.		ω	Ξ.	٠,	w.	w.	u,	41	w.		٠.	٠:	٠.	٧.	$\stackrel{\smile}{\cdot}$		٠.	13.95	e.	<u>۲</u>	œ	22.99	٠.	٠.	14.84	13.93	_
1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	•	1.00	•	•	•	1.00	•	1.00	•	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00		1.00		1.00	
2.42	2.60	3.34	29.706	8.82	9.47	9.	7.94	7.97	8.05	6.75	74	54	54	14	83	. 78			•	•	•	25.540	25.014	25.167	24.413	23.074	22.355	22.422	24.106	23.932	23.167	1.81	0.94	0.8	2.29	3.25	2.42	21.757	0.92	22.646	2.72
.68	•	•	-7.378	•	•	•	-6.684	•	•	. 62			ú	. 65	.97	•	-10.605	•		•	•	-14.329	•	-16.618	•	•	•	•	. 28	-11.979	. 21	.77	.01	.49	-14.208	-13.699	-15.320		87	-9.530	.08
.31	7.510	8.603	10.911	10.126	(1	12.717	14.075	14.095	15.492	13.403	852	.338	.463	.631	. 922	.469	.487	.089	.967	.325	.657	.645	.929	.848	15.749	. •	•	14.719	16.117	17.262	ᅼ	.45	14.246	æ	ω.	3.02	14.307	.77	6.54	15.154	.33
541	541	1 541	1 541	3 541	1 542	A 542	1 542	A 542	1 542		A 542		A 543		A 543									A 544						A 544	A 545	54	A 545	54	54	54	A 545	54	Ŋ	ゼ	4
ASN Z	ASN A					LEU		LEU	LEU	LEU	LEU	LEU	Ħ	THE	TH	THR	THE	THR	開	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	GLU	GLU				GLU	GLU	GLU.	GLU	MET	MET
2	ODI	NO.	ບ	0	z	ď	CB	Ď	8	CD2	ט	0	z	ජ	CB	061	CG2	บ	0	Z	ð	ප	ව්	8	NE	ZZ	NHI	NHZ	ບ	0	z	ð	g	Ď	8	OE1	OE2	ບ	0	×	S
1255	1256	1257	1258	1259	1260	1261	1262	1263	1264	v	1266	1267	1268	1269	1270	1271	1272	1273	1274	1275	1276	1277	1278	1279	1280	1281	1282	1283	1284	1285	1286	1287	1288	1289	1290	1291	1292	1293	1294	1295	1296
A TOM	ATOM	MOTA	ATOM	ATOM	ATOM	ATOM	ATOM	MOTA	ATOM	MOTA	MOTA	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

	איסטטטטטטאסטע מיסטטטטטאסטע
	. <i>v</i> . æ 4. rv. <i>v</i> . <i>v</i> . <i>v</i> . æ æ æ æ
11.00 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
	0004464444
-7.478 -5.997 -6.831 -7.727 -8.454 -9.068 -9.080 -7.727 -9.080 -9.080 -7.911 -9.080 -9.683 -9.481 -9.683 -9.683 -9.683 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9.080 -9	25 25 25 25 25 25 25 25 25 25
0 8 5 5 5 4 4 6 1 1 6 8 8 8 8 6 8 8 8 7 7 1 8 8 8 8 8 8 8 8 8 8 8 8 8 8	
~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	5549 550 550 550 550 550 550 551
MET A MET A A B A B B B B B B B B B B B B B B B	***********
SG CG	
1299 1299 1399 1300 1300 1300 1300 1310 1311 1321 1322 1323 1323	1328 1328 1333 1333 1333 1335 1335 1333
ATOM ATOM ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM ATOM

GLU A 551 GLU A 552 GLU A 553 GLU A 553 GLU A 554	ບ	ບ	บ	ບ	0	0	ט	0	z	ບ :	ט	U	ບ	Z	ບ	Z	Z	U	o	Z	υ ·	ซ	ល	ບ	0	N	ບ	U	ບ	บ	0 (0	U	0	z	ບ	U	U	Z	O.	Z,	ັບ
CA GLU A 551 23.714 -6.493 22.297 CG GLU A 551 25.312 -8.358 22.922 CD GLU A 551 25.312 -8.358 22.922 CD GLU A 551 25.312 -8.358 22.922 CD GLU A 551 25.312 -8.358 23.196 OEZ GLU A 551 25.312 -8.358 23.136 OEZ GLU A 551 25.315 -10.617 24.325 OC GLU A 551 25.475 -6.418 20.897 O GLU A 551 25.475 -6.48 20.897 O GLU A 551 25.475 -6.935 20.728 N ARG A 552 24.128 -6.750 18.529 CG ARG A 552 24.128 -6.750 18.529 CG ARG A 552 24.128 -6.750 18.529 CG ARG A 552 24.128 -6.7583 16.190 CC ARG A 552 24.128 -6.750 18.249 CC ARG A 552 24.128 -6.750 18.249 CC ARG A 552 24.128 -6.750 18.249 CC CX ARG A 552 27.664 -8.435 15.999 NH1 ARG A 552 27.773 -7.319 13.901 C ARG A 553 22.447 -7.818 14.969 CC CX A 553 22.447 -7.818 14.969 CC CX A 553 22.477 -1.106 CX A 553 22.477 -1.119 13.901 CC CX A 553 22.477 -1.119 13.901 CC CX A 553 22.467 -1.106 CX A 554 25.107 -2.420 18.243 CC CX A 553 22.480 -2.420 18.243 CC CX A 554 26.265 -2.570 CC CX A 554 26.265 -2.599 CC GLU A 554 26.267 -2.959 CC GLU A 554 26.211 -3.111 2.4.903 CC GLU A 554 26.217 -2.886 24.688 CC GLU A 554 26.217 -2.886 CC GLU A 554 26.217 -2.886 CC GLU A 554 26.207 -2.424 23.280 CC GLU A 554 26.207 -2.424 23.280 CC GLU A 554 26.207 -2.424 23.280 CC GLU A 554 26.217 -2.886 CC GLU A 554 26.207 -2.424 23.280 CC GLU A 555 26.917 -2.886 CC GLU A 555 26.917 -2.899 CC GLU A 555 26.917 -2.898 CC	.00 7.3	.00 7.4	.00 11.1	.00 12.9	.00 13.8	.00 12.2	.00 7.9	.00 8.1	9.8 00.	.00 10.1	.00 12.4	.00 20.8	.00 27.0	.00 30.0	.00 34.4	.00 30.2	.00 34.6	00.	.00	. 00.	. 00.	. 00.	. 00.	. 00.	. 00.	9 00.	8 00.	.00	.00	.00	.00 15	.00 14	ထ	6 00.	8 00.	.000	9 00.	.00	0	0	0	7
CA GLU A 551 23.714 -6.49 CG GLU A 551 25.312 -8.35 CD GLU A 551 25.312 -8.35 CD GLU A 551 25.376 -9.85 OEI GLU A 551 25.376 -9.85 OEI GLU A 551 25.376 -9.85 OEI GLU A 551 25.783 -10.216 C GLU A 551 25.784 -7.40 CG ARG A 552 24.128 -6.75 CD ARG A 552 24.128 -6.75 CD ARG A 552 24.128 -6.75 CD ARG A 552 27.060 -7.85 NH2 ARG A 552 27.064 -9.43 NH2 ARG A 552 27.064 -1.70 C CYS A 553 22.384 -7.81 CC CYS A 553 22.384 -7.81 CC CYS A 553 22.384 -2.128 CC CYS A 553 22.384 -2.128 CC CYS A 553 22.384 -2.136 CC CYS A 553 22.284 -1.10 CC CYS A 554 26.211 -3.11 CC GLU A 554 26.211 -3.11 CC GLU A 554 26.211 -3.11 CC GLU A 554 26.211 -2.136 CC HIS A 555 28.487 -6.22 CC HIS A 555 28.487 -6.22 CC HIS A 555 28.487 -6.22 CC HIS A 555 28.242 -8.41 CC HIS A 555 29.024 -7.97	2.297	2.907	2.922	3.196	4.325	2.287	0.897	0.720	9.888	8.529	7.595	6.190	690.9	4.969	4.950	5.999	.901	920.	•	•	•	•	•	•	•	ö	。	ö	ش	4.	4. O	9	.5	0.3	9.7	9.1	8.8	0.0	0.09	1.28	2.05	21.319
CA GLU A 551 CG GLU A 551 CG GLU A 551 CD GLU A 551 OE1 GLU A 551 OE2 ARG A 552 CG ARG A 552 CG ARG A 552 CG ARG A 552 CG ARG A 552 CC ARG A 553 CC ARG A 554 CC CYS A 553 CC CYS A 553 CC CYS A 553 CC CYS A 553 CC CYS A 554 CC GLU A 554 CC GLU A 554 CC GLU A 554 CC GLU A 555 CC HIS A 555 CC CC CC HIS A 555 CC CC HIS A 555 CC	6.49	7.84	8.35	9.85	10.21	10.65	6.41	5.93	6.84	6.75	7.40	7.58	.37	.81	. 85	8.43	7.31	5.29	5.02	.38	.97	2.14	2.42	2.48	1.70	.95	.55	Ţ.	-2.42	-2.88	-4.11	-2.03	99	.32	.18	.73	. 22	.08	.41	. 92	.97	-6.808
CA GLU A CG GLU A CG GLU A OE2 GLU A OE2 GLU A OE2 GLU A OE3 GLU A OE3 GLU A OE3 GLU A OE3 ARG A OE3	3.71	3.89	5.31	5.37	5.78	5.01	4.34	5.47	3.61	4.12	3.14	3.64	4.95	5.73	7.06	7.6	7.7	4.3	'n.	'n.	έ.	$\dot{\circ}$	0.75	4.89	5.70	'n	ø.	ů.					7.57	8.59	7.56	8.73	8.48	8.60	8.24	8.52	9.02	29.094
	Ø	A	₹ 4	⋖	ø	A	ø	ď	ď	ď	ø	ď	ø	ø	ø	ø	ď	ø	ø	ď	4	æ	K	ø	Ø	4	Ø	Ø	ø	Ø	ø	ø	ø	ø	Ø	ď	ø	ø	ø	ø	ø	S S
	ć	5 5	_	_	_	Ī	_	0	7 N	_				•																								9 CG	.—	_	-	0 CD2
ATOM ATOM ATOM ATOM ATOM ATOM ATOM ATOM	7.	7 =====================================	7 6	7 5	13	13	13																						-	-	-	_		-			-	-	М	-	_	ATOM 138

																																		•	_			_	_	_	
	ρi	•	•	: ,	N	9	2.8	2	23.17	3.5	5.89	6.78	4.95	o.	•	•	۰.	•	۰.	3.84	ų	7.02	ω.	•	ω.	•	5.34	9	3.43	. 7	3.49	ı.	•	6.19		•	3.03	٥.	•	2.00	2.00
1.00		•	. ·	•	۰.	0	٥.	1.00	ö	۰.	1.00	1.00	1.00	1.00	۰.	1.00	1.00	1.00	1.00	1.00	1.00	1.00	•	1.00	٠	•	1.00	•	1.00	•	0.	۰.	1.00	۰.	۰.	1.00	1.00	1.00	1.00	1.00	1.00
7.8	7.4T	٠.	. y .	5.03	•	4.25	.04	.76	9	.61	7	15.400												21.619				•	.04	15.983		14.562	æ	14.299	. 74	-1	•	14.708	.76	12.287	ġ.
m (n .	ω (2.78	7.4	.08	.47	-3.879	•	-4.276	-3.226	-1.417	-0.835	-0.890	•	•	•	•	•	0.279	1.023	-0.732	-1.072	•	-1.673		•	•	•	-2.102	•	.80		99.	-5.820	.37	•	.51	•	0.509	-	ų.
90	0.23	8.04	28.312	7.06	6	5.42	.91	23.632	22.735	.25	.79	29.447	4.	•	•	•			ö	31.301		ς.	o.	31.501	ä		ë	₹.	32.417	3.26	2.67	1.36	0.72	0.78	30.122	3.64	1.77	2.72	9	.84	1.56
HIS A 555	₹ '	∢ ;	Ø,	A	ď	Ø	ø	ARG A 556	ARG A 556	ø	ď	Ø		ø	_	ø	ď	ø	ø	ø	Ø	ď	ø	ø		ø	MET A 558	4	ø		ø	4	GLU A 559	Ø	ø	ø	ø	Ø	ď	SER A 560	26
ບ	0 !	z i	ජ (8	ဗ္ဗ	8	NE	CZ	NH1	NH2	ບ	0	×	đ	g	CG1	CD	CG2	บ	0	z	ಕ	9	හි	SD	S	ບ	0	×	ସ	g	ც	8	OE1	OE2	ບ	0	z	g	g	ဗ္ဗ
1381	1382	1383	1384	1385	m	1387	1388	1389	ന	ຕ	m	സ	39	1395	ന	1397	1398	1399	4	1401	1402	1403	1404	1405	1406	1407	1408	4	1410	4,	1412	1413	1414	1415	1416	1417	1418	1419	42	1421	4
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

1.00 1.00 1.00 17.530 15.806 18.810 16.884 15.316 16.308 16.638 17.793 17.292 18.648 19.378 14.016 11.390 10.050 16.393 18.231 11.192 14.911 15.101 5.109 5.921 4.535 4.973 3.777 2.881 1.796 4.193 3.756 4.693 4.095 1.214 2.948 3.804 3.601 2.532 1.694 5.825 6.253 7.145 7.290 6.068 6.044 31.119 31.326 31.879 31.979 33.259 33.863 33.768 35.073 36.208 36.208 35.434 35.881 37.222 38.273 39.083 39.083 37.786 34.969 31.566 30.004 32.200 34.290 34.350 SER A 560
LEEU A 561
LEEU A 562
ALA A 562
ALA A 563
TRP A 563 CZZ 1425 1428 1429 1430 1431 1432 1433 1434 1435 1436 1437 1438 1439 1440 1441 1442 1443 1444 1445 1446 1447 1448 1449 1450 1451 1452 1453 1454 1455 1456 1457 1458 1459 1460 1426 1427 1462 1461 L463 ATOM ATOM

• ·	Ä	ບ :	ບ ເ	υ (0 (0 1	ָט י	0	z	O	ບ	0	ບ	0	Z	ບ	ບ	ບ	บ	ບ	0	Z	ပ	ບ	ບ	ບ	ບ	ပ	0	z	ບ	ບ	ບ	ບ	ບ	ບ	ບ	ပ	U	O.	Z
	0	4,	4	_	12	ω	4	9 00	300	00	4,	τU	.00 4.42	41	4	マ	4	41	.00 3.92	4	.00 5.03	Ŋ	ഗ	Ŋ	8	0	<u>ი</u>	9	7	98.9 00	0	0	0 6.7	7.0	0 7.8	0 7.5	ų.	0.5.0	0 9.1	0 10.	ų.
.301 1.	.600 1.	.356 1.	67 1.	.633 1.	.582 1.	.592 1.	.835 1.	5.518 1.	.365 1.	Η	.709 1.	Н	Н	H	+-1	Н	33 1	1 1	27 1	~	Н	Н	Н	∺	Н	Н	-	Н	i	19.739 1.	ι.	H	۲.	Ή.	572 1.	679 1.	528 1.	292 1.	418 1.	.765 1.	÷.
2.519	1.357	12.194	12.235	10.859	9.768	10.766	11.762	12.257	10.892	10.379	8.890	8.341	11.092	11.220	11.423	12.087	12.119	12.026	11.141	11.300	11.860	9.997	9.185	7.839	6.643	5.968	7.041	9.780	9.766	10.317	10.808	.136	.923	.914	.757	.573	.556	.719	975	12.193	7
34.856	3.05	α	ö	0	0	28.798	31.929	31.067	32.752	32.472	32.849	32.554	33.115	34.332	32.300	32.786	31.550	30.425	30.859	33.922	4,	m	വ	ゼ	35.662	Ø	v	ဖ	~	36.860	œ	ä	œ.	39.368	ď	•	ų.	37.377	ιί	39.718	4.
	ASP A 566		•		ø			ø	ø		SER A 567	Ø		ø		ď			ø	PRO A 568	Ø	ď	LEU A 569	Ø	•	4	LEU A 569	ø	LEU A 569	•		K		PHE A 570		PHE A 570	PHE A 570	PHE A 570	PHE A 570	A 5	ASP A 571
						•																z	ð	පු		9	CD5	ບ		N			ප -	_	_			CDS	ט	0	×
146	1466	1467	1468	1465	1470	1471	1472	1473	1474	1475	1476	1477	1478	1479	1480	1481	1482	1483	1484	1485	1486	1487	1488	1485	1490	1491	1492	1493	1494	1495	1496	1497	1498	1499	1500	1501	1502	1503	1504	1505	1506
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

20.35 37.48 15.89 20.46 22.46 24.95 25.51 31.74 36.07 17.39 14.11 9.92 12.90 18.15 15.55 6.14 18.35 16.97 12.31 23.88 15.08 15.22 15.07 21.46 1.00 1.00 1.00 1.00 11.00 11.00 11.00 11.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 21.136 24.760 25.401 25.224 26.845 28.301 28.181 22.425 23.373 22.098 22.628 20.020 26.532 25.954 23.745 22.767 23.290 22.296 24.685 21,114 24.850 21.393 23.983 24.705 23.898 24.800 14.789 18.197 13.802 15.353 15.079 17.213 9.968 9.090 7.746 6.981 8.825 11.088 10.949 12.192 13.190 13.946 14.149 16.241 10.127 10.761 14.242 10.963 12.322 11.657 9.247 41.059 40.876 39.394 39.020 37.544 36.639 39.959 39.857 42.098 41.435 42.414 42.272 42.087 43.280 43.072 44.287 44.345 43.302 38.703 37.023 37.111 36.028 35.809 35.722 40.376 40.645 39.068 12.221 38.461 38.945 37.838 LEU A 572
LEU A 572
LEU A 572
LEU A 572
LEU A 573
LLE A 573 574 575 575 575 575 575 574 574 574 574 572 572 LEU A ELEU A ELE LYS LYS LYS LYS LYS LYS LYS GLN GLN GLN GLN GLN ASP ASP ASP 1545 1543 1544 1524 1525 1526 1527 1529 1530 1531 1532 1533 1533 1534 1536 1537 1538 1539 1540 1541 1542 1518 1519 1520 1522 1523 1516 1517 1521 1512 1513 508 ATOM ATOM

38 .1.0	44 1.00 28.1	353 1.00 27.2)24 1.00 29.7	346 I.00 23.3	785 I.UU 31.3	138 1.00 32.4	924 1.00 32.4	390 1.00 31.1	501 1.00 28.8	806 1.00 29.9	174 1.00 25.3	028 1.00 33.6	875 1.00 33.0	663 1.00 35.4	239 1,00 36.4	817 1,00 36.5	337 1.00 38.8	. [4 00 [30]	000 T 000 T	708 1.00 #4.0	751 1.00 36.8	813 1.00 13.	537 1.00 13.	317 1.00 14.	153 1.00 17.	424 1.00 12.	701 1.00 12.	159 1.00 10.	190 1.00 8.	033 1.00 9.	352 1.00 8.	256 1.00 9.	770 1.00 7.	379 1.00 5.	028 1.00 6.	633 1.00 6.	930 1.00 7.		121 1.00 12.	850 I.00 4.	273 1.00 3.	859 1.00 4.	.104 1.00 6.
11.655	10.312	9.371	11.452	11.186	11.566	11.424	11.456	10.514	9.097	8.118	6.691	12.556	12.565	13.534	949 41	900 91	000.04	10.200	15.800	16.976	14.554	9.547	9.256	9.648	9.799	7.811	6.982	7.546	6.265	6.374	6.834	4.968	5.785	4.625	6.694		100	00/./	8.717	5.841	4.809	6.477	5.969
2.28	41.622	2.63	3.77	4.50	4.21	5.61	5.75	2 7			, 6	, 4	ָרְילָ מילי	, u		, è		۰ و	7.0	5.2	6.5	9	8	7	9	m	00		<i>y</i> ,		i C	7		, u			. v	ר. ע	۵. ص	3.4	3.2	4.6	5.7
S S	A 576	A 57	A 57	A 57	A 57	7	, L	1	ה לו	4	∢ ι	ດີເ ≰ເ	Ωi N	ת לו	₹ i	Α .	Ą	N N	Ŋ 2	A 57	A 57	B 64	1 th	ם ק	ם ק	1 T	ם מ	9 6	ָ מַנ	מ מ מ	d b	3 6	, p	9 6	9 (ם מ	B 64	B 64	B 64	B 64	B 64	B 64	9 B
_	5 B	og	ט	C) 2	4 É	5 8	<u> </u>	පු (8	E E	NZ	บ	O	z	ජි	9	ß	OD1 ASP	OD2) 2	3	5 8	3 8	3 c		o :	z	5 (CB THR	5 6		י כ)	Z	ð			C SER	O SER	M	ð
•	1550		•	1 (, ,	7 1	, ,			• •	• •	•	• •	•	•																						158	158	158	159	159	159	M 1593
Ę	ATOM PTOM			2016		ATO	ATON	ATO	ATO	ATO	ATOM	ATOM	ATO	ATOM	ATO	ATO	ATOM	ATOM	ATOM	MOT &		ALOM	ATO	ATOM	ATO	ATOM	ATO	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATC	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	MOTA	ATOM

0.000000000	4 6 W 0 L O C	2 4 6 6 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			
28.058 27.214 25.743 27.433 28.634 27.846 29.958 30.458	0.27 0.27 0.27 0.05 0.06 0.06 0.60	7.4. 8. 7. 8. 8. 8. 8. 8. 8. 8. 8. 8. 8. 8. 8. 8.	
6.981 6.586 6.400 7.685 7.685 8.653 8.653 8.191 8.191	40 8 4 4 8 9 9 6	-0.408 -0.812 -0.418 -0.418 1.774 2.604 2.357 2.062 2.284 2.284	-0.415 1.031 0.270 0.988 1.741 1.076 1.737 3.096 3.679 3.087
8.0. 4.4.1. 2.0. 2.0. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3.4.1. 3	0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.0	31.444 33.590 33.553 33.796 33.940 33.947 32.763 33.988 35.175	999 999 999 999 999 999 999 999
дамидада		LEU B 649 LEU B 649 LEU B 649 PHE B 650	н п п п п п п п п п п п п п п п п п п п
1594 1598 1598 1598 1600 1600 1600	1 1 6 0 6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1611 1612 1613 1614 1615 1616 1617 1619 1620 1621	333333377777
ATOM ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM ATOM

26.566 26.388 27.623 27.531 28.518 28.518 28.071 24.665 24.528 23.240 22.582 21.425 22.068 23.425 22.517 24.579 26.019 25.925 24.712 24.654 25.839 24.769 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 4.7. 44.399 4.399 4.3194 4.3194 4.3194 4.3194 4.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3196 6.3 36.925 36.925 36.770 36.116 36.103 35.793 34.602 34.713 34.803 34.039 32.592 31.683 30.444 29.457 29.069
34.665
34.668
35.172
35.172
37.138
37.162
37.606
38.644 41.074 41.943 42.195 43.039 41.577 38.074 36.417 **мимимимими** 1641 1642 1643 1644 1645 1646 1648 1649 1650 1651 1652 1653 1654 1655 1656 1657 1659 1669 1660 1663 1664 1665 1666 1667 1668 1669 1670 1671 1672 1637 1638 1639 1673 1674 1675 1640 1676 1677

8.10 8.59 14.10 8.68 9.00 12.41 10.91 5.96 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 00.1 L.00 00.1 1.00 22.548 21.663 22.601 22.205 24.491 25.495 25.164 20.556 20.884 19.981 24.463 25.146 25.433 20.156 20.924 21.405 22.595 24.133 24.006 20.658 22.174 24.087 22.293 23.612 20.640 19.460 21.465 28.707 24.362 21.632 -15.803 -10.196 -10.806 -13.070 -13.017 -12.143 -9.422 -13.629 -14.579 -14.296 -12.090 -9.905 -12.435 -6.470 -8.824 -9.615 -10.769-12.110 -7.388 -8.168 -7,045 -8.820 -7.943 -8.416 -7.226 -9.999 -8.056 -11.188 -8.885 35.270 39.996 35.494 41.822 42.353 39.591 36,976 35.439 37.054 37.057 42.608 37.773 39.850 40.775 42.087 40.511 39.143 40.177 39.053 36.065 38.156 38.893 37.004 39.271 32.951 39.093 34.794 36.009 33.118 32.700

629 629 9 659 659 659 659 659 659 659 659 628 659 659 658 658 657 658 658 657 657 657 959 657 ф ø ф LEU LEU LEU LEU LEU LEU TYR ALA TYR TYR TYR TYR TYR TYR TYR TYR TYRALA ALA LEU LEU LEU ARG CDS 989 0 z g 1716 1712 1713 1714 715 1717 1708 1709 1710 1711 1706 1707 1703 1704 1705 1698 1699 1700 1701 1702 1688 1689 1690 1691 1692 1693 1694 1695 1696 1697 1686 1687 1685 1682 1683 1684 ATOM ATOM

		1.00 1
7.653 7.915 7.178 6.983 6.983 6.053 6.053	17.273 18.735 18.462 19.265 20.086 20.086 20.086 20.082 20.082 20.086 22.090 22.666 22.388 23.284 19.340 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271 17.271	17.03
08 -11.793 29 -11.304 86 -10.027 72 -9.762 73 -8.629 84 -7.652	38.479 38.625 -14.338 39.508 -12.879 40.902 -13.230 41.803 -12.308 43.286 -12.110 44.132 -12.325 43.829 -12.854 41.198 -14.658 40.287 -16.291 40.059 -16.291 40.059 -17.727 38.985 -18.274 41.057 -18.320 40.143 -17.268 36.059 -16.930 38.274 -17.868 36.076 -18.315 39.059 -16.930 39.059 -16.930 39.059 -18.201 39.059 -18.315 39.059 -16.882 36.076 -18.315 39.095 -19.335 39.095 -19.208 40.700 -16.171 39.932 -14.082 38.978 -16.273 41.816 -18.142	3.727 -118.38

 ATOM
 1720
 CB
 ARG
 B
 661

 ATOM
 1721
 CG
 ARG
 B
 661

 ATOM
 1722
 CD
 ARG
 B
 661

 ATOM
 1723
 NE
 ARG
 B
 661

 ATOM
 1724
 CZ
 ARG
 B
 661

 ATOM
 1724
 CZ
 ARG
 B
 661

 ATOM
 1726
 NH2
 ARG
 B
 661

 ATOM
 1726
 NH2
 ARG
 B
 661

 ATOM
 1729
 N
 LEU
 B
 662

 ATOM
 1729
 N
 LEU
 B
 662

 ATOM
 1739
 CA
 LEU
 B
 662

 ATOM
 1739
 CA
 LEU
 B
 662

 ATOM
 1749
 CG
 LEU
 B
 663

 ATOM
 1749
 CG
 LEU
 B
 663

 ATOM</t

20.39 17.26 19.29 15.39 17.46 17.36 15.48 18.34 18.42 20.70 18.65 17.97 18.36 17.77 18.28 12.51 16.34 19.46 18.39 18.41 19.07 20.80 19.53 23.37 22.67 20.67 18.31 1.00 1.00 1.00 1.00 1.00 1,00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 14.376 15.484 16.035 12.850 14.819 15.012 15.127 13.122 13.988 13.001 10.861 10.606 15.382 15.007 13.477 22.277 18.009 21.937 17.291 17.387 16.166 15.341 14.616 13.896 13.950 12.412 11.029 13.553 15.762 14.568 -21.576 -24.235 -22.126 -22.508 -21.979 -22.817 -22.454-22.369 -21.891 -21.858 -21.419 -20.972 -21.407 -22.719-23.613-21.630 -21.413-19.999 -19.874-20.771-18.385 -21.649 -22.131-21.320 -21.450 -20.070 -20.549 -21.680 -23:085 -23.691-20.191-23.15140.005 37.477 15.058 34.778 43.433 42.191 16.559 15.892 47.206 47.828 42.257 36.292 42.651 15.104 41.170 40.404 42.450 15.677 17.699 18.413 42.463 42.273 40.892 39.851 44.255 44,105 43.167 40.586 42.019 41.558 41.330 38.775 34.094 43.206 8.698 699 699 699 669 699 669 670 670 670 668 899 668 699 699 670 999 667 667 667 667 667 667 667 667 667 668 ARG LEU ARG ARG ARG ARG LEU LEU LEU GLU GLU GLU ARG ARG ARG ARG LEU LEU LEU LEU LEU GLU GLU GLU GI'I LEU LEU LEU С С С О 0 666 NH2 OE2 NH1 NE CG CG NA NH1 9 5 8 8 1799 1789 1790 1796 1798 1800 1775 1776 1778 1779 1783 1784 1785 1786 1787 1788 1792 1793 1794 1795 1797 1802 1769 1770 1772 1773 1774 1777 1780 1782 1791 1801 1766 1767 1768 1771 1781 ATOM ATOM

0000	ង ប ប ប	000	0.020	OUZ	טאט	ROUG	υυυυ	ROU	υυυτ) O O O O Z O O O
1.00 22.45 1.00 23.79 1.00 24.29	.00 25.9 .00 25.9 .00 27.1	0 36. 0 34. 0 40.	.00 25.1	2.7.8	3.6	00 21.8 00 21.7 00 20.7		.00 18. .00 18.	.00 18. .00 18. .00 19.	1.00 16.34 1.00 16.34 1.00 17.58 1.00 16.20 1.00 16.44 1.00 15.70
17.484 16.227 17.765	6.64 6.63 5.22 7.22	12.787 12.135 12.247		17.308 16.035 14.874		19.255 19.131 20.274		9 4 7	444	20.188 20.560 19.085 21.548 22.121 20.250 19.469
-25.575 -26.222 -25.084	5.74	6.66 5.63 7.60	37.	-21.670 -22.304 -22.309		2 2 2 2		.39 84 84	31.	-20.376 -21.410 -20.283 -17.940 -16.886 -18.030 -16.803
45.665 45.803 48.081	0000	. 42 11. 05	1400	52.507 52.982 52.982 52.234	52.909 54.075 54.142	54.146 50.904 50.723 50.422	49.579 49.540 49.687		99 51 27	54.239 53.642 54.824 51.657 51.382 51.143
B 671 B 671 B 671		B 672 B 672 B 672		B 673 B 673 B 673	B 673 B 673		B 674 B 674 B 674 B 674		B 675 B 675 B 675	
SER I				HIS H						GLU B GLU B GLU B GLU B GLU B LEU B
8 8 c	្ត ទី <u>២</u> ខ	8 8 8 8	a Suosi	3 8 8 E	SE2	oo z	5886	Boos	5 5 5	CB C C C C C C C C C C C C C C C C C C
1804 1805 1806	1808 1809 1810	1811 1812 1813	1815 1816 1816	1819 1820 1820	1822	1825 1825 1826 1826	1828 1829 1830	1832 1833 1834	1835 1836 1837	1838 1839 1840 1841 1842 1844
ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM	ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM

12.95 12.55 11.65 13.20 11.61 1.00 16.02 1.00 15.51 16.19 13.66 1.00 14.28 1.00 16.75 1.00 18.50 1.00 17.30 15.38 13.66 14.37 13.46 13.27 14.08 17.27 14.06 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 00.1 1.00 17.076 19.860 20.652 16.468 21.826 20.210 18.110 21.623 18.958 22.248 20.884 21.105 20.660 27.580 23.184 23.578 27.418 21.520 23.765 26.257 28.220 22.666 21.847 25.031 22.098 23.901 -11.289 -9.776 -11.481 -11.675 -12.922 -11.903 -10.987 -13.349 52.940 -12.548 -14.175 -12.585 -11.445 -13.393 -12.439 -12.466 -13.689 -14.274 -13.422 -11.904 -14.733 -16.530 -14.467 -13.318 -16.590 -15.737 48.355 51.758 50.914 47.473 50.019 49.721 53.840 54.959 51.018 50.072 49.162 53.795 48.616 50.907 49.775 49.895 48.062 49.142 48.698 49.611 44.427 48.841 45.378

680 679 679 679 679 679 619 678 678 678 678 678 677 677 677 HIS B д д д ф ф ш HIS B GLU B ф GLU B m ILE TER ILE TLE TE TE TPE ILE HIS] TLE HIS HIS HIS HIS HIS GLU CE1 NE2 CD5 8 1 1 1 1 **OB1** OE2 0 2 5 8 8 8 8 1880 988 1879 1881 1882 1883 1884 885 1878 1875 1876 1877 1869 1870 1871 1872 1873 1874 1868 1864 1865 1866 1867 1863 1860 1862 1858 1859 1861 1856 1855 1857 1853 1854 1847 1848 1849 1850 ATOM ATOM TOM ATOM ATOM

8.14 10.57 12.34 12.34 12.34 12.34 10.05 10.07 10.07 10.07 10.03 10.35 10.35 10.35 10.35 10.35 10.35 10.41 10.35 10.43 18.371 17.912 17.831 18.174 23.783 25.083 24.780 24.780 22.486 22.486 22.486 22.136 22.282 22.282 22.431 22.897 23.316 23.316 23.723 21.858 22.192 23.723 21.858 22.192 21.858 22.192 21.858 19.089 19.208 -6.158 -5.766 -6.971 -6.775 -5.561 -7.674 -7.845 -4.661 -5.428 -6.900 -5.949 -6.672 -5.923 -6.590 -4.513 -8.596 -7.521 -8.757 -7.629 -8.117 -6.939 -7.671 -6.984 -7.210 -8.851 45.365 43.963 43.516 42.232 41.368 48.710 49.523 50.887 50.760 51.776 49.522 50.010 50.485 51.117 50.646 48.706 48.706 46.291 46.818 43.188 TRP B 681

TRP B 682

THR B 683

LEU B 684

PHE B 684 1900 1901 1902 1903 1904 1906 1906 1910 1910 1910 1918 1918 1920 1920 1921 1923 1924 1926 1926 1927 1895 1896 1897 1898 1899 1889 1890 1891 1892 1893

6.86 5.59 6.24 7.58 8.36 6.00 6.00 8.56 7.39 10.18 7.27 13.68 11.42 7.09 17.34 1.00 1.00 22.883 24.062 25.193 26.139 22.475 22.972 21.036 21.085 20.687 19.723 18.791 16.252 19.017 18.692 20.069 19.119 19.673 21.068 20.897 19.676 20.772 19.791 20.934 21.897 0.139 -0.907 -1.890 -3.058 1.309 0.473 -1.302 -0.557 -1.518 -2.196 -0.754 1.429 2.012 1.084 0.303 -0.238 -0.747 -1.748 47.388 47.428 48.116 45.030 45.360 45.965 46.488 43.227 43.962 43.666 42.153 41.445 45.871 45.839 44.898 46.448 47.531 47.058 46.784 48.012 51.758 52.481 52.355 51.509 48.443 688 688 688 688 688 688 688 689 689 689 687 687 687 687 687 687 686 686 687 686 686 686 686 686 686 GLN GLN GLN GLN GLN 開開 HIS HIS HIS 1965 1966 1967 1962 1963 1964 19946 1947 1948 1950 1951 1952 1953 1953 1957 1959 1960 1945 1940 1942 1943 1944 1938 1939 1941 1935 1936 1937 1932 1933 ATOM ATOM ATOM ATOM ATOM ATOM ATOM

10.36 13.10 11.49 27.49 28.02 27.57 11.32 9.71 12.17 15.72 18.87 12.33 11.26 10.21 10.93 12.97 16.35 22.86 15.98 9.33 11.74 17.749 18.968 12.529 16.015 15.881 14.644 14.262 17.925 19.276 18.465 19.800 20.038 20.368 17.054 15.982 20.641 16.481 16.037 16.071 2.5. 4. 6. 6. 4. 6. 6. 4. 6. 6. 4. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 9.751 5.846 6.125 10.421 44.790 445.130 447.273 443.456 443.342 443.342 443.993 443.221 443.221 443.221 443.221 443.221 443.221 443.221 443.221 443.221 443.221 443.221 443.221 49.655 49.287 50.129 48.200 47.670 47.629 48.418 49.824 50.583 51.722 46.173 45.826 45.346 43.892 43.246 43.781 43.456 43.952 д д ддд ф ф ф 1978 1979 1980 1982 1983 1984 1985 1986 1987 1988 1990 1991 1992 1993 1994 1995 1996 1998 1999 2000 2001 2002 2003 2004 2002 2006 2008 2009 1975 1976 1977 1981

		• .	,	
4.81 6.55 7.27 7.22 7.22 7.22 7.88	44.04.00.00.00.00	6 5 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	446000000000	8 6 7 4 4 4 7 7 7 8 8 7 7 7 7 7 7 7 7 7 7 7
11111111111111111111111111111111111111				
	12.616 12.705 12.159 11.947 11.978 11.848 12.043 13.185 13.177	10.866 10.866 10.909 10.909 8.563 8.563 9.309 9.309	8.060 9.890 9.890 8.510 8.239 8.809	6.818 8.817 10.881 11.830 10.687 11.467
4407640	3.212 4.874 5.925 7.200 8.469 9.744 10.900 111.587 12.606	3.5869	3.257 2.779 1.431 1.335 1.672 1.300 2.334 3.260	3.272 4.171 0.423 0.785 -0.843 -1.862
	38.662 40.219 39.358 40.136 39.302 40.166 39.304 39.133 38.279	38.683 37.374 37.374 36.620 36.238 36.238 36.238	36.893 37.458 37.458 39.362 39.962 41.414 42.223 42.863	42.877 43.498 37.198 36.474 36.758
0000000				6 6 9 8 8 8 8 8 9 9 9 9 9 9 9 9 9 9 9 9
LEU B MET B MET B MET B MET B MET B	• • • • • • • • • • • • • • • • • • • •			ARG HARG HARG HARG HIS HIS HIS HIS
o g g g g g o	N C C C C C C C C C C C C C C C C C C C	CG C	CRUCGBS	NH1 O O C CA C CA C CA C CA C CA
2014 2015 2016 2017 2018 2019 2020	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	2003 2003 2003 2003 2003 2003 2003 2003	2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	04 00 00 00 00 00 00
ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM ATOM	ATOM ATOM ATOM ATOM ATOM

υ;	ą U	×	บ	Ö	0	z	U	บ	U	U	บ	ບ	0	z	ບ	ບ	ບ	0	0	ບ	0	z	ບ	ບ	บ	ບ	0	Z	ບ	0	z	ບ	ບ	ບ	ပ	ບ	ບ	0	Z	ບ
4	• •	2.00	۰.	. 7	ທ	3.99	ų.	•	•	•	2.00	•	•	•	5.27	6.51	8.63	8.97	12.11	5.92	4.87	6.01	6.04	5.99	5.27	4.96	4.27	3.80	•	•	ŭ	6.51	3	7.52	. 7	5.38			8.61	. 7
1.00	. 0	1.00	•	•	0.	۰.	٥.	•	H	H		નં	H	Н	Н		۲	Н	_	П	П	1.00		Н	-	1.00	1.00	1.00	1.00	1.00	۰.	1.00	٥.	1.00	°.	1.00	•	1.00	1.00	1.00
11.034	2 2	50	.75	.40	. 04	. 60	. 59	15.713	17.177	17.919	17.322	14.019	14.340	13.188	12.691		13.051	14.300	12.634	_	\Box	\circ	10.068	9.202	8.644	8.079		7.135	•	•	•	•	•	•	.51	.10	ú	.56	13.720	4.32
.76	- 4	00.	-3.935	.62	. 94	96.	.65	.03	-4.058	-5.193	-4.198	96.	-5.385	•	-6.958	-7.724	-8.161	-8.095	-8.568	•	•	•	-5.398	•	-4.192	•	-1.797	•	.24	-5.756	-4.594	-4.450	•	•	-1.541	-3.807	. 7	-6.094	-6.586	o.
. 35.058	ى 5 د	33.306		.70	. 79	22	96	01	46	36.714	ď	- 2	Ø	37.737		37.055			34.860	39.392	40.241		ιÜ.	0.7	œ.	38.418	•	4.	•	•	.89	43.105	.91	.14	42.183	.83	4	63	8	61
HIS B	HIS B		HIS B	HIS B	HIS B 699	LEU B	LEU B	LEU B	LEU B	LEU B	LEU B	LEU B	LEU B	ASP B	ASP B	ASP B	ASP B	ASP B	ASP B	ASP B	ASP B	GLN B	GLN B	GI'N B		GI'N B	GITN B	GIN B	GI'N B	GLN B	ILE B	ILE B	ILE B	ILE B	ILE B	ILE B	ф	m	MET B 704	MET B 704
- '	57 ND1		60 CD2		62 0								0 0 0 0												5 CG												4 D	2	9 9	_
M 2056				M 2061					M 2066			N	7	~	7		7	73	7		M 2078				4 2082										7		7	7	505	7
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATO	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATON	ATOM	ATON	ATOM	ATON	ATOM	ATOM	ATOM	ATOM	ATON	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

																																			٠						
7.41	9.47	7	2.92	ū	8.07	7.84	9.	ω.	•	ü	7.0	•	4.	٥.	ø.	ω. Γυ	4.	œ.	ų.	o.	4.	۳.	ú	ဖ	7			6.1	7.6	9.3	ο.	8.0	ů	8.1	18.22	٥.	0:7	9	2.8	23.73	
1	1.00	•		°	°	٥.	•	1.00	1.00	1.00	1.00	1.00	1,00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	۰.	1.00	0	0:	۰.	•	•	۰.	1.00	1.00	1.00	٥.	1.00	1.00	1.00	1.00
727 772	. 4	5.7	•	3.3	3.7	4	1.2	0.0	7	8.683	ο.	0.8	0.5	.80	0.48	. 17	.46	1.59	1.29	12.848	3.87	5.24	.46	3.80	.99	.50	13.401	.08	•	.49	.48	.29	•	. 12	.98	. 79	7.533	.68	.5.520	4	•
Ľ	-9.941	0.90	10.8	-8.835	9.37	٥.	.98	15	0		.28	9.46	0.2	. 14	. 55	6.05	9	-	-7.837		•	۲.	•	o,	-9.959	ö	•	2.85	-12.592	3.57	•	-12.174	.72	-11.675	-11.742	-11.027	.21	-12.285	-12.431	-11.520	-11.706
,	41.418	. 60	9.20	•	4.40	42.825	.40	42.471	1.13	0	ത	44.763	45.637	44.936	46.226	46.091	45.622	47.299	48.520	46.870	47.837	47.296	47.061	.27	49.474	~	47.649	•	45.246	43.770	44.439	48.674	49.789	•	49.206	48.600	ω.	49.134	49.811		51.492
707	704 704	704	704	704	704	705	705	705	705	. 502	705	705	705	206	206	206	206	706	706	707	707	707	707	707	707	708	708	708	708	708	708	708	708	709	709	709	0	709	709	709	402
	MET D	MET B	MET B	MET B	MET B	MET B	MET B	MET B	MET B	MET B	MET B	MET B	MET B	CYS B	CYS B	CYS B	CYS B	CYS B	CYS B	SER B	SER B	MET B	MET B	MET B	MET B	MET B	MET B	MET B	MET B	TYR B	TYR B	TYR B	TYR B	TYR B	TYR B	TYR B	TYR B				
8	3 5	8 6	8 8	ט	0	N	ජ	ච	និ	SD	CE	บ	0	z	S	g	SG	ບ	0	z	5	CB	90	บ	0	z	g	GB	g	SD	CE	บ	0	N	g	g	ဥ	CD	CEI	Z	НО
(2000	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	12	2128	2	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139
E	ATOM	MOTA	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

26.16 26.08 23.68 23.93 26.62 25.92 26.01 27.09 27.73 31.65 37.06 27.09 26.93 26.49 25.93 20.88 17.41 22.99 21.61 17.84 17.96 17.95 17.36 17.08 11.000 11.000 11.000 11.000 11.000 11.000 11.000 11.000 11.000 1.00 1.00 1.00 1.00 1.00 1.00 00.1 1.00 13.160 11.736 12.437 13.427 12.651 14.334 13.431 9.272 8.055 7.008 5.640 10.157 14.067 9.970 12.496 11.571 11.516 10.875 10.631 13.783 11.615 12.455 16.319 15.796 16.876 14.417 13.049 9.676 11.024 11.349 12.271 11.848 13.493 16.632 -10.659 -13.072 -12.677 -13.241 -11.968 -11.816 -9.365 -13.092 -12.463 -11.436 -11.607 -12.565 -12.666 -14.544 -15.029 -12.746 -9.239 -14.237 -13.097 -10.673 -15.179 -15.723 -11.494 -13.122 -13.303 -12.930 -10.643 -10.107 -10.280 57.790 56.900 58.181 57.697 52.808 53.214 52.091 50.569 54.430 55.390 54.392 55.467 55.171 54.261 54.847 54.896 56.913 56.825 53.453 52.745 53.705 54.827

713 713 713 713 714 714 714 714 714 ILLE B CYS B LYS B VAL VAL LYS VAL VAL VAL VAL ILE ILE ILE IIE IIE HE 2164 2165 2166 2167 2167 2170 2171 2174 2175 2176 2161 2162 2163 2160 2157 2158 2159 2154 2155 2156 2152 2153 2145 2146 2148 2149 2150 2151 142 2143 ATOM

31.40 30.98 33.01 31.76 32.36 33.96 33.35 34.12 32.76 32.07 33.60 34.05 33.06 34.30 31.30 33.04 32.68 32.92 32.42 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 3.278 5.664 10.820 6.682 6.764 8.871 5,434 4,661 5,035 7,795 9.353 9.616 9.035 7.739 6.831 7.672 13.859 12.22 9.860 11.204 11.142 12.311 13.620 10.504 9.773 9.764 8.516 -16.776 -17.409 -16.934 -17.908 -19.452 -20.482 -19.601 -19.329 -18,114 -20.326 -20.122 -20.614 -17.846 -17.477 -19.604 -18.826 -18.778 -19.624 -18.581 -18.641 -17.488 -18.965 -15.941 -17.991 -15.622 -17.067 -16.882 -16.647 -16.343 49.590 50.012 52.432 17.220 49.586 53.501 53.906 53.353 51.469 51.974 53.839 51.249 54.251 53.776 54.148 52.865 54.031 54.799 55.411 56.060 60.847 57.395 61.153 57.185

B 718 719 719 717 716 716 715 715 716 716 716 ILE B ASP B ASP B LEU LEU LYS LYS LEU LEU LEU LEU ASP LEU ASP ASP ASP ASP TEE HI IIE ITE ILE ITE ASN ASN ASN GG2 GG2 GB CG1 8 8 8 9 6 6 8 8 6 6 2220 2215 2216 2218 2219 2221 2214 2213 2212 2200 2201 2202 2203 2204 2205 2206 2206 2209 2210 2211 2199 2198 2195 2196 2197 2194 2193 2190 2191 2192 2189 2185 2186 2187 2188 2184 2183 ATOM TOM ATOM ATOM

0.379 1.00 39.2 0.944 1.00 38.6 4.896 1.00 30.2 5.592 1.00 30.0 4.368 1.00 29.0 4.578 1.00 28.0	4 10 0 0 0 10 4 4 4 4 4 4 5 5 1 1 1 1 1 1 1 1 1 1 1 1	
18.08 18.85 15.85 16.37 14.64	4.870 -11. 4.870 -11. 4.870 -11. 6.885 -10. 6.885 -10. 7.017	
CE LYS B 72 NZ LYS B 72 C LYS B 72 O LYS B 73 N PHE B 73 CA PHE B 73	2230 CB PHE B 721 2231 CG PHE B 721 2233 CE1 PHE B 721 2234 CZ PHE B 721 2235 CE2 PHE B 721 2235 CE2 PHE B 721 2235 CC2 PHE B 721 2236 CC2 PHE B 721 2237 C PHE B 721 2238 O LYS B 722 2240 CA LYS B 722 2244 CE LYS B 722 2245 CG LYS B 722 2245 CG LYS B 722 2245 CG LYS B 722 2246 C LYS B 722 2246 C LYS B 722 2247 O LYS B 722 2249 CA LYS B 722 2249 CA LLE B 723 2250 CB LLE B 723 2251 CG1 LLE B 723 2251 CG1 LLE B 723 2252 CG1 LLE B 723 2255 CG1 LLE B 723 2255 CG1 LLE B 724 2256 CG LLE B 724 2256 CG LLE B 724 2257 CA LLE B 724 2256 CG1 LLE B 724 2257 CA LLE B 724 2256 CG1 LLE B 724 2257 CA LLE B 724 2256 CG1 LLE B 724 2256 CG1 LLE B 724 2257 CA LLE B 724 2256 CG1 LLE B 724 2257 CA LLE B 724 2256 CG1 LLE B 724 2257 CA LLE B 724 2256 CG1 LLE B 724 2256 CG1 LLE B 724 2257 CA LLE B 724 2256 CG1 LLE B 724 2256 CG1 LLE B 724 2256 CG1 LLE B 724 2257 CA LLE B 724 2256 CG1 LLE B 724 2257 CG1 LLE B 724 2256 CG1 LLE B 724 2257 C	
44444	ATOM ATOM ATOM ATOM ATOM ATOM ATOM ATOM	

24.25 14.79 18.29 12.47 15.28 21.11 13.39 12.91 11.86 13.37 13.34 12.87 11.24 1.00 12.86 1.00 13.02 1.00 1.00 1.00 1.00 1.00 1.00 1.00 00.1 00: 7.977 9.111 9.856 11.018 10.272 9.455 10.030 8.777 8.493 9.289 10.738 8.785 9.663 6.428 6.590 3.194 3.682 5.067 4.079 35.496.-15.203 34.562 -15.001 -15.598 -15.706 -16.311 35.308 -10.766 -11.875 -10.794 -10.222 -9.074 -15.040 -13.739 -12.497 -16.195 -17,440 -18.653 -18.547 -19,089 34.085 34.579 34.356 36.036 36.773 35.355 34.034 37.716 35.323 36.101 36.061 37.769 38.621 39.394 37.235 37.560 36.915 38.182

728 728 728 728 728 728 728 729 ALA B LYS LYS LYS TYR] TYR TYR TYR TYR TYR TYR ALA ALA TYR TYR TYR TYR ALA CD7 G G G 2305 2306 2300 2301 2302 2303 2298 2299 2296 2297 2284 2285 2286 2287 2288 2289 2290 2290 2292 2293 2294 2295 2283 2280 2282 2277 2278 2279 2281 2276 2275 2273 2274 2272 2271 ATOM ATOM

15.27 18.51 17.81 19.79 22.24 26.72 31.50 31.30 20.57 19.49 18.10 18.38 17.76 22.19 11.15 15.53 15.48 16.47 17.37 21.62 28.05 21.53 22.67 18.53 18.27 14.75 16.47 18:15 17.05 14.65 13.31 8.91 1.00 11.000 11.00 11.00 11.00 1.00 11.00 1.00 1.00 1.00 900000 11.429 13.008 12.326 11.762 12.620 12.293 13.462 13.863 13.400 13.870 14.614 14.608 10.568 10.626 8.210 10.986 14.022 15.072 14.367 7.676 6.466 9.274 13.196 13.501 -16.150 -13.937 -15.085 -15.313 -15,685 -15.595 -16,164 -12.894 -11.520 -10.622 -9.962 -11.070 -13.853-13.592 -10.792-10.387 -11.463 -11.751 -9.967 -11.924 -11.610 -12.798 -11.198 -11.898 -10.096 -8.272 27.732 28.075 31.403 32.343 30.998 34.775 30.649 28.578 29.366 31.179 32.243 34.636 30.846 30.276 30.555 31.036 33.125 35.586 29.874 28.444 30.066 27.003 29.161 28.964 30.392 32.132 30.027 28.931 30.646 39.805 LEGU 1
LEGU 1
LEGU 1
LEGU 1
PRO E
PRO B
PRO B
PRO B
PRO B
HIS B HIS MLA MLA MLA MLA VAL ASP LEU LEU LEU LEU LEU VAL VAL 2329 2316 3318 2319 2320 2323 2324 2325 2326 2328 2331 2332 2333 2334 2335 2336 2337 2338 2339 2340 2342 2344 345 346 2314 2315 2317 2321 2322 2327 2341 2343 2347 2313

1.00 16.15 1.00 17.06 1.00 10.98 1.00 12.04 1.00 13.84 1.00 13.62 1.00 14.68 1.00 12.99 1.00 12.99 1.00 12.84 1.00 12.84 15.45 16.07 1.00 16.42 1.00 27.73 1.00 13.09 1.00 13.18 1.00 11.57 1.00 10.08 2.00 8.74 19.47 15.56 14.71 20.16 1.00 34.03 30.86 1.00 1.00 1.00 1.00 1.00 0.479 1.912 3.098 4.439 4.879 2.013 3.986 2.175 5.527 4.109 4.089 2.518 3.756 3.389 4.984 5.951 7.711 8.356 4.634 4.455 7.332 3.145 2.769 2.789 3.090 3.100 -7.289 -7.259 -7.256 -5.661 -7.314 -7.514 -8.893 -12.157 -11.832 -10.775 -5.946 -6.349 -10.029 -11.414 -6.403 -10.348 -6.472 -6.065 -6.653 -5.162 -2.096 -3.607 -5.959 -7.793 -6.424 -8.799 -4.035 -3.181 -13.248 36.550 37.279 38.107 38.063 37.348 38.449 38.338 38.926 33.648 35.757 36.728 37.616 36.976 34.999 34.206 35.063 34.224 30.615 35.257 33.095 31.857 30.162 32.132 30.887 32.672 34.771

738 738 739 739 739 739 737 737 737 737 GLU B GLU B THR B THR B THR B THR B THR B PHE B PHE B PHE B PHE B PHE B PHE B Ø GIN B GLUB GLU B PHE PHE LYS GIM B PHE PHE PHE PHE PHE 2387 2388 2389 2386 2369 2370 2371 2372 2373 2374 2376 2376 2377 2378 2384 2385 2382 2383 2381 2368 2365 2366 2367 2364 2362 2363 2360 2361 2359 2355 2356 2353 ATOM ATOM

117.49 20.53 20.53 23.74 22.67 19.74 19.74 23.62 26.76 31.98 31.99 33.87 33.87 115.61 114.70 115.05 114.19 114.19 113.97 113.97 113.99 113.99 113.99 113.99 113.99 113.99 113.99 114.08 115.17 116.23 116.23 116.23 116.23 116.23 LYS B 740

ARG B 741

IEBU B 742

VAL B 742

VAL B 742

VAL B 742

IEBU B 743

IEBU B 743

IEBU B 743

IEBU B 743

IEBU B 744

IIEB B 744 2395 2396 2397 2398 2399 ATOM ATTOM A

34.47 336.86 331.35 331.35 331.35 331.35 331.35 331.35 331.35 331.35 331.35 331.35 331.35 41.77 25.04 23.53 23.64 21.89 21.89 21.59 119.85 -0.614 -0.281 -1.034 1.439 2.266. -0.115 -0.373 -0.373 -0.373 -0.373 -1.625 -1.509 -2.600 -3.728 -0.701 -0.701 -0.350 -0.350 -0.457 6.091 6.109 4.934 5.225 4.026 3.391 9.502 9.880 8.364 8.925 8.974 8.424 7.839 10.125 10.735 10.153 11.772 6.586 2.138 3.607 3.607 2.621 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 1.007 4.135 10.472 446.120 43.011 42.0123 42.033 42.033 42.033 33.031 42.125 33.033 33.020 40.035 41.370 33.020 33.020 40.025 41.666 42.782 33.030 33.030 40.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 33.030 LIVS B
LIVS B
LIVS B
LIVS B
LIVS B
CGLU B
GGLU B
GG 2449 2450 2451 2458 2459 2460 2461 2462 2463 2463 2464 2466 2466 2466 2467 2469 2469 2470 2471 2471 2473 2448 2452 2453 2454 2455 2455 2456 2440 2442 2443 2445 2446 2447 2438 2439 2441 2444 2436

Z	ບ	ບ	ບ	0	0	ပ (0	Z	ບ	ບ	0	ပ		Z	ບ	ບ	ט	ບ	U	ט	0	Z	ບ	ပ	U	Ü	O	ບ	0	Z	U	U	O	D	O	0	Z	ບ	O	ບ	ບ
0	.00 18.	.00 19.0	.00 20.5	0 15.5	20.	0 17.8	0 18.	0 16.	1.00 15.69	.00 14.	.00 15.	.00 15.5	.00 15.0	15.2	.00 15.3	.00 14.4	0 15.8	.00 12.6	.00 14.2	.00 15.9	.00 16.8	.00 15.3	.00 15.0	16.4	.00 17.7	.00 17.4	17.1	.00 14.9	0 15.5	.00 14.1	.00 13.	13.7	.00 13.7	0 13.4	.00 13.1	.00 12.7	.00 12.	.00 11.7	.00 12.2	1.00 9.65	0 11.6
.86	. 53	.87	-3.312	.67	۲.	. 58	. 54	-1.023	-0.198	.97	-0.953	.13	.31	2.083	•	4.387	•	6.917	•	•	•	2.186	•		•	•	•	•	2.189	•	•	•	•	.93	•	86	2.528	۲.	.55	5.917	.03
-0.837	•	9	Н	.31	ú	.11	.92	7.	-5.478	-6.578	-6.392	9	-4.346	-6.147	-5.968	-6.937	4.	-7.320	4	-6.089	-5.642	-6.656	-6.847	-7.795	-9.193	-10.051	-7.928	-5.512	-5.155	-4.772	.49	-2.757	ų.	'n	-2.657	.88	-2.832	.08	. 28	-1.641	.25
4.0	41.111	ū	2.9	.68	43.496	.06	9.0	41.534	N	4	43.683	ĸ.	۲.	42.142	•	4	9.	•	42.760	•	44.984	•	•	•	•	•	•	•	47.876	•	46.811	ď	ĸ.	45.829	46.863	φ.	.86	φ.	44.564	•	44.648
B 75	щ	Д	ф	ф	ф	B 750	æ	M		B 751	B 751	_	B 751	B 752	B 752	B 752	B 752	B 752	щ	ф	ф	m	ф	B 753	B 753	B 753	B 753	B 753	B 753	B 754	B 754	B 754	B 754	B 754	B 754	B 754	B 755	B 755	B 755	B 755	B 755
N ASP	CA ASP	CB ASP		OD1 ASP	OD2 ASP	C ASP	O ASP				OG SER			N ILE			CG1 ILE									CD1 ILE				N VAL	CA VAL	CB VAL	CG1 VAL	CG2 VAL	C VAL	O VAL	N PHE	CA PHE	CB PHE	CG PHE	CD1 PHE
47	2477	47	2479	2480	2481	482	483	484		486	487	88	489	90					2495											2506	2507	2508	2509	2510	2511	2512	2513	2514	2515	2516	2517
ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

14.19 15.33 15.54 19.68 14.85 15.14 13.60 13.76 13.54 15.82 14.24 14.24 13.20 12.81 12.98 16.30 16.18 18.19 12.46 18.26 21.98 17.21 20.75 14.12 13.48 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 3.300 1.984 2.177 2.783 1.680 3.141 3.198 2.942 2.646 1.603 0.387 6.030 7.066 6.414 8.4417.687 8.297 5.673 5.123 5.791 3.867 3.823 4.899 6.035 -6.683 -7.161 -7.628 -4.170 -6.181 -6.197 -7.156 -3.564 -2.764 -3.374 -4.070 -5.537 -6.363 -1.860 -1.162 0.667 2.869 0.251 1.178 2.331 1.515 5.675 51.320 52.419 50.210 50.310 50.167 50.628 48.450 50.933 52.012 53.166 51.935 50.782 50.386 51.213 51.516 51.770 52.778 50.851 49.283 49.516 49.204 47.751 47.457 47.378 47.725 49.697 49.792 49.688 49.988 PHE PHE PHE PHE PHE PHE TYR TYR TYR TYR TYR TYR TYR VAL PHE 2540 2541 2542 2543 2518 2528 2529 2530 2532 2533 2534 2535 2536 2537 2538 2539 2544 2545 2546 2547 2548 2549 2550 2551 2552 2553 2555 2556 2557 2520 2524 2525 2526 2527 2531 2522 2523

1.00 14.87 1.00 13.04 1.00 13.09	.00 13.8 .00 13.8	0 16.	.00 21.	.00 24.5	.00 33.0	.00 22.	.00 22.00	.00 23.7	.00 27.7	.00 32.	.00 34.	.00 36.2	21.0	.00 21.7	2	.00 23.1	.00 27.0	.00 31.6	300.	.00 36.6	.00 40.0	.00 22.1	.00 19.7	0 22.8	.00 23.2	0 23.4	.00 24.3	24.2	.00 24.2
	. 89 . 66 . 46	10.217 8.426	.45	.20	4.6	56		12	.71	_	.65	. 53	10.247	0.01	11.232	1.40	2.78	2.93	49	3.6	1.69	2.43	3.43	•	3.38	'n.	4.09	13.885	5.52
-2.965 -2.591 -3.188	3.4.6.	1 0 0	2.30 3.14	000	.78	1.13	.00	2.123	•	•	•	•	2.236	•	•	•	•	•	9 7	.78	.91	.94	2.537	.61	.26	0		7	.48
8.41 7.38 7.23	r	, 8 3 3 2 5	.79	. 0	55.132	54.647	53.381	53.913	53.783	55.041	55.947	55.071	54.985	52.815	52.622	H	ö	તં લ	•	. œ	œ.	m.	•	'n	ω.	Ŕ	H	50.013	તં
B 760 B 760 B 760	9 9 9 9	ששם	9 9 9	B 761 B 761		B 761	B 762	B 762	B 762	B 762	B 762		B 762 B 762		В 763	В 763		B 763	ъ 763	B 763	В 763	В 763	7	B 764	76	16	9	B 764	
CG PHE CD1 PHE CE1 PHE	CE2 PHE CD2 PHE						NI GLN		GEN GEN				GLN				CG ARG		NE ARG	Н	~	ARG	ARG	LEU	A LEU	CB LEU	•	 H	CD2 LEU
562	0 10 10 10 0 10 10 1 4 10 10		0 0 0																			2594 C	2595 C	2596 N			599	0	601 (
ATOM ATOM	ATOM ATOM		ATOM				ATOM						ATOM							ATOM				ATOM			ATOM	ATOM	ATOM

											•																										•						
ທ	9:	.5	7	8	7	4.	4	9.	0.						י ע י		•		י ע	۳; ش	٠: س	6			4	4	2		. 9		35.45	4,		 	38.55	•	•	`•	45.30	42.90	40.93	41.56	
00	00.	00.	00.	00.	00	00	00	00	0	3 6	3 6	3 6	3 8	3 6	9 6	3 6	3 6	90.	00.	00.	00	00.	00.	00.					0	1.00	1.00	•	0		0		0	٥.	1.00	1.00	1.00	1.00	
13.193	14.089	12.032	11.719	10.464	10.240	91.9	7.693	7 597	0000	770.77	175.51	13.2/3	14.424	14.840	13.698	15.802	15.610	16.119	16.083	17.232	17.768	18.837	18.545	20.094	16.985	17.816	15.863	15.625	14.268	14.309	12.981	13.834	15.698	S	15.505	15.523	15.082	13.896	4.2	2.57		6.9	
0.99	71	8		10	, <)	ין קר. קיני די		D . T	1.40	2.42	. 24	[_ '	.34	1.96	0.87	1.56	9.80	່ທ	1.02	8	2.94	1.4	3.0	3.8	S.	9.	7	4.9		<u>.</u>	ณ์	-6.786	Ē	4	H,	6	98	7	7.	-6.789	
6	, u	י אינו	מיים		4. 6	, ,		,	4, 1	. 75	.25	. 12	96.	. 82	9	<u>.</u> و	. 6	.44	ق	9.	9.	ŏ	5	7	6		~		9	7		9	7.5	7.6	9.6	9	0	1.86	2.4	1.06	0.37	61.022	
	#0/	# 0 / # U I	765	697	765	765	765	765	765		-		766		. 994	166	166	166	191	•	•	٠	•	•	•	•	-	00/0	-	20, 4		_	_	B 768		B 769		97. 5	694	97. 6	69.6	3 769	
	מ היון י			•			•	LYS B	• •	٠.	LYS B	THR B	THR B	THR B	THR B	THR B	THR B	THR B	ASN B	A NO. B	• •	•			D NOW		• •	4 5 5				•			LEU		•	1.11.1	1.17.1				
		•						• •			٠.		_		_										אַ מַ	ى ر	>	z (5 8	9 5	3 5	797	່ວ	C) 2	٤ 5	5 8	3 5	3 8	9 6	ל	ס כ	,
;	0	09	2604	0	0	0	2608	0	Н	Н	H		Н	્ન		H	Н		5	1 5		4 6	Ž (Ž i	Ž Č	ž :	7 9	× 5	3 6	ש נ	7632		. 6		3 6	3 6	2 5	3 6	ה ה ה	# 5	# 5	2643	1
	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	MOTA	MOTA		ATOM.	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	MOTA	MOTA	NO.	E OF A	1016 1016	ATOUR MOUNT		ATOM.	ATOM	ATOM	ATOM	

טט	ບ ບ	0	Z C	ه د	Z	ບ	ບ	ບ	ບ	U	ບ	0	ບ	ບ	ບ	0	Z	ပ	บ	ပ	0	z	ນ	ບ	0	ပ	0	×	Ö	ບ	0	ບ	ບ	0	×	ັບ	บ
000	4 00.	.00 41.	.00 43.	41.8	.00 42.	42.	41.8	38.4	1.00 37.30	35.2	.00 34.3	1.00 34.71	.00 3	1.00 35.17	.00 44.	.00 43.3	46.1	1.00 48.39	.00 48.	.00 50.3	.00 50.0	1.00 52.64	.00 54.6		۰.	00.	.00 56.5	1.00 57.80	.00 59.1	2.65 00.	.00 60.2	.00 59.8	.00 59.	.00 59.4	0 59.5	.00 59.	0.59.9
7.93 9.30 0.34	21.762	3.66	22.090	9.61	9.14	19.229	8.77	9.35	20.662	21.169	•	.75	19.	18.576		18.	17.	16.	15.	17.42	17.17	18		20	21,1	0	.455	.768	20.328	19.901	. 4ı	55	21.875	.533	2.433	.861	24.393
ល កុំ 4	-5.41	-6.0	74	-7.74	-7.46	-8.88	. 14	•	æ æ	-7.42	-6.43	ا. ا	-6.332	-7.191	-9.775	-10.968	-9.181	-9.932	-9.113	-10.356	-11.413	-9.510	-9.794	1 -8.723	-9.024	1.17	1.44	-12.031	-13.397	-14.164	-13.432	-14.219	-13.436	-14.440	-12.330	-12.203	-10.968
9.98 0.28 9.36	59.450	.06	57.116	. 07	•	œ.	.18	.17	55.729	54.776	54.263	53.309	54.703	55.641	59.572	59.703	60.235	61.159	61.590	62.368	. 95	. 74(.884	. 02]	.106	63.691	. 63	64.709	64.694	65.990	67.155	66.138	64.527	64.836	64.043	63.800	64.540
	GLN B 770 GLN B 770	Ø	GLN B 770	ам	ф		M	Д	Щ	TYR B 771	æ	щ	Д	ф	TYR B 771	ф	æ		m	pa		ф	щ	ф	ф		щ	æ	ф	Д	ф	B 77	R B 774	R B 774	щ	m	GB 775
	8 8 8 8	_	NEZ C	_	_																		CA SER	CB SER	OG SER	C SER	O SER	N THR	CA THR	_	-	CG2 THR	_	_	N ARG	•	CB ARG
2644 2645 2646	2647 2648	649	2650	652				929	657	658					2663		2665				2669					674	675	9/9	677	678	619	680		682	683	684	2685
ATOM ATOM ATOM	ATOM ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

51.05 51.62 52.75 51.07 49.65 45.78 56.28 55.27 55.36 56.03 56.21 54.10 53.82 47.40 44.67 45.46 52.28 57.92 57.74 59.27 59.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 27.199 27.483 27.780 26.856 25.369 29.916 27.460 27.595 27.702 24.271 24.291 24.508 27.466 26.983 28.117 28.526 25.464 26.737 28.693 27.413 26.219 25.804 26.817 26.404 25.321 24.117 25.217 25.546 -8.680 -8.103 -7.751 -6.263 -7.973 -7.020 -9.548 -9.228 -9.548 -10.950 -11.020 -11.917 -13.324 -12.007 -8.480 -7.367 -9.364 -5.930 -6.018 -13.372 -9.569 -11.793 -10.338 -10.887 -11.173 -10.337 -13.431 -12.077 -12.663 -12.614 -13.471 -5.532 -11.452 53.553 53.599 51.739 54.508 53.774 54.098 53.361 52.748 52.486 51.867 59.846 60.560 56.810 55.960 56.128 57.514 55.525 61.659 58,638 57.078 56.561 57.807 56.916 58.011 57.189 62.577 54.233 PRO B PRO B PRO B PRO B PRO B PRO B THR B THR B THR B THR B THR B THR B LEU B LEU B LEU B LEU B LEU B LEU B щщ LEU LEU SER SER SER SER SER SER PRO PRO PRO PRO PRO PRO PRO PRO ARG ARG PRO ARG ARG ARG ARG 2715 2716 2718 2719 2720 2723 2724 2725 2717 2721 2722 2704 2705 2706 2707 2708 2709 2710 2712 2713 2714 2695 2696 2698 2699 2700 2701 2702 2703 2694 2697 2693 5688 689 2690 2692 5687 2691 ATOM

0 2 0 0	υυυς) Z U C	טטט	000	Z ()	ນ ບ ເ	ט ט כ) Z C	ບໍ່ບໍ່ເ	Z	o z	ບບ	0;	ຊ ບ	บบ	Ü	u ا	ບເ) Z
1.00 39.24 1.00 40.30 1.00 40.49 1.00 40.18	.00 40. .00 40.	.00 40.9 .00 41.1	1 4 6 6	.00 41.4	.00 41	.00 41.6	.00 43.0	.00 45.6	.00 49.0	.00 53.8	.00 54.7 .00 54.8	.00 53.7	.00 49.4	.00 50.0	00 51.6	.00 54.3	.00 50.7	00 51.	00 52.4
28.080 29.555 30.355	0.10	9 9 9 9	$ \frac{1}{2} $	2.6	3.96		.41	1.70	90.5		.12	32.04	8	07	.56	.34	.34	64 0	2.8
-9.353 -7.730 -8.528 -7.626	9 9 9 9	10.14 10.59	12.12 12.60 12.47	9 9 9	-9.749	.08	. 4. 4 7. 10. 0	101	10.50	5.4 4.0	.06	7.7	3.29	υ <i>'</i>	2.46	13.00	3.42	.65	 ! M
8.38 7.99 7.06		5.40 4.17	4.16 5.32 5.02	92	m m	7.00	200		,	מ	8.3	0.0		7.7.	4	5.33	7.58		5.31
	3 781 3 781 5 781			. [- [-	1- 1-		- 1- 1	- [- [- [- [1		785	8		σ α	786
SER B PRO B PRO B	PRO B PRO B PRO B						PRO B	HIS B		ກເທ		HIS B		TLE B	ILE B			ILE B	PRO B
G G S C	8800	g z g	8 6 6 8	ဦ ၁ ၁ ၁	cs s	88						0000					25	ບເ	
2728 2729 2730	2732 2733 2734 2734	2736	2738 2739 2740	2741 2742 2743	2744 2745	2746	2748	2751	2753	2754 2755	2756	2758	2760	2761	2763	2765	2766	2767 2768	2769
ATOM ATOM ATOM	ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM ATOM ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM

42.69 39.49 53.49 52.06 53.17 51.86 50.85 53.54 47.69 47.41 47.97 48.35 49.77 48.66 46.60 42.24 44.51 31.47 29.48 49.91 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 25.896 28.897 28.935 28.970 28.477 37.659 31.289 34.239 36.339 38.706 38.601 31.252 34.527 34.591 35.449 39.864 33.745 32.535 32.878 34.063 33.165 29.991 30.109 27.910 26,866 26.932 28.288 28.269 35.163 33.817 -6.478 -13.716 -15.489 -16.389 -13.883 -14.207 -14.357 -15.300 -15.772 -15.024 -16.887 -12.983-12.893 -11.911 -10.565 -8.262 -7.805 -14.416 -13.138 -12.649-13.428 -14.750 -12.880 -16.882 -14.544 -15.482-13.727-15.085 -14.044 30.090 22,180 23.030 24.423 22.266 22.987 24.541 23.458 22.417 25.177 25.766 26.093 25.145 25.408 30.457 30.468 24.418 24.583 31.223 30.807 20.931 26.077 24.287 25.516 24.676 30.480 30.063 786 787 787 787 787 787 787 787 787 787 М дη **д д д д д д д** ARG ARG LEU LEU LEU LEU LEU LEU LEU LEU LEU ARG ARG ARG ASP ASP ASP ASP ASP ASP ASP TYR TYR TYR TYR TYR TYR TYR TYR 002 2799 2800 2808 2809 2793 2794 2795 2796 2797 2798 2801 2802 2803 2804 2805 2806 2807 2810 2812 2789 2790 2792 2811 2813 2775 2776 2778 2779 2780 2781 2782 2783 2784 2785 2791 2774 2777 ATOM ATOM

.

.

•

				•																	•													-				٠
	יט נ	ָט נ	Z (S	Ü	υ	0	X T	י ט	D.	ບ	b	บ	O	U	U	Ö	0	N	ບ	Ü	0	z	ŭ	ซ	ບ	ບະ	ບ	O	0	×	ບ	O	υ	ŭ	0	0	
0 29.	.00 24.5	0 25.7	.00 30.2	00 2	.00 2	.00 22	.00 2	.00	.00 20	.00.	.00 16	.00 14	.00 13	.00	0 10	.00 11	.00 21	0 21	.00 21	.00 21	.00 22	.00 21	.00 23	25	.00 25	.00 26	.00 24	.00	.00 26.5	.00 25.3	1.00 28.49	0 31.	.00 32.	.00 38.	.00 44.3	00 47	.00 44.5	
	000		2. c	ຜູ້ຜູ້	. თ	2.	υ.	.5	2	3.49	٠.	.91	. 63	.57	_:	3.08	76	99.	17	.46	. 58	7	.9		9	90.	13	. 23	6.32	6.47	. 24	•	88	7.88	.25	38.639	8.15	
-10.01 -10.23 -9.33	0 0	-7.	φ 1	7 9	9	-7	φ	-7	9	-	•	-	-	•	•	•	•	-6.195						-1.497	-	_	-		_	_	-							
26.471		, 0	<u> </u>	O 0	-	m	m	m	~				~		:			·.		~	Ξ.	~:	÷	:	:	۳.		:	<u>.</u>	9.4	0.4		2.2	3.1	4.6	o,	5.4	
ω ω 4·	1414	41 4 1	4	4 4	4.	4	4	D.	വ	ហ	വ	Ŋ	Ŋ	ហ	Ω.	Ŋ	Ŋ	ហ	9	v	ဖ	9	7	7	7	7	7	7	7	7	ထ	ω	æ	00	80	80	co	
TYR P TYR P HIS P		o o	ß	HIS P											PHE P								LEU P								GLU P	GLU P	GLU P	GLU P	GLU P	сги р	GLU P	
OOE	: 5 E	පු සි	ND1	CE1	8	ບ	0	z	ව	g	ပ္ပ	CDI	CEJ	CZ	CE2	CD2	ບ	0	Þ	CA	ບ	0	z	g g	g	ς Ω	9	CD5	ບ	0	Ż	S S	GB	ຍ	8	OEI	OE2	
2815 2816 2817	2818	2819	2821	2822	2824	2825	2826	2827	2828	2829	2830	2831	2832	2833	2834	2835	2836	2837	2838	2839	2840	2841	2842	2843	2844	2845	2846	2847	2848	2849	2850	2851	2852	2853	2854	2855	2856	
ATOM ATOM ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	

94

24.35 19.40 17.35 17.40 16.80 31.00 27.90 24.46 26.02 26.05 21.13 18.44 16.45 31.42 30.01 29.07 26.65 1.00 19.86 17.74 16.52 17.71 17.18 17.84 32.17 33.47 18.51 17.44 1.00 1.00 1.00 1.00 1.00 0000000 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 37.748 37.875 38.516 38.005 35.719 34.230 35.380 41.209 41.240 40.138 38.922 36.852 36.631 36.281 38.653 36.161 34.567 31.684 42.934 42.153 36.401 32.979 37.535 34.805 12.418 7.051 7.769 7.527 -2.607 -4.028 3.806 2.024 2.791 2.303 2.612 2.296 2.296 2.296 3.296 3.395 3.855 5.788 5.785 5.785 5.785 5.785 5.785 5.785 5.785 5.785 5.785 5.763 0.429 0.276 6.275 -5.978 -0.254 1.696 2.598 5.451 9.313 10.693 -4.084 29.073 33.486 31.853 27.603 26.905 25.766 25.582 26.404 24.458 22.680 22.353 23.048 21.913 28.826 27.826 31.459 32.325 24.156 24.535 24.899 28.018 27.685 30.033 29.895 30.205 29.353 29.952 24.443 28.185 27.131 Pu Pu GLU TIE GLY GLY GLY GLY TE ITE ILE E E GLU GLU GLY GLY OE2 GG 12 GG 12 GG 13 2886 2888 2889 2890 2892 2893 2869 2875 2876 878 2879 2880 2881 2882 2883 2885 2887 2894 2895 2896 2863 2864 2865 3866 2868 2870 2871 2872 2873 2874 2877 2884 2891 2897 2862 2867 ATOM ATOM

22.46	, ,	4		7 . C	4 7 7 7		7.7	1 6 4 C	14.	17.7	18:	7.0	7 6	7 L		0 0	0 0	2 6	20.7	200	22.	4.0	22.	2 6		4 4	23	24	26.	26.	29	; ;		. 4	ָ הַ רָּ		·	٠ ١
0	> (O	O	> <	0	> <	9	0 (9	0	0	0	٠ ر	, ,	، ر	٠, ١	٠,	٠ ر	_ `	٠,	٠, ١	٠ `		: -		: -		, –	1.00		9				, (7	· '	?
٠i,	7.	Ξ;		7.	4 4			7	9.	5.	Ņ	ä	7	m i	0	i-i i		-	φ̈́	٠ <u>.</u>		ا ش		4 1			ָ קייי		1 0				- C	υ. υ.	7.7		ر د	ທຸ
11.610	0.68	2.55	9.31	46	30	67	62	25	76	90	70	26	0	8	0	S O	58	33	37	61	0.21	1.58	5 6	0.93	89	20 6	J 1	קיי	107.11	ŕċ	ء ڊ م	7	9	0	7.	_ ,	6	ις.
. 12	.03	.84	. 22	.53	7.	55	.41	96.	.56	9	8.	8.	9.	.38	.48	, ,	9.	.2	.2	9.	7.4	7.1	9.		9	٠. ج	٦	9 1	25.144	# ! - !	ហ		٠. ٦	٠. د	0.0	9.1	0.0	o.5
14	14	М	-	Н	Н	Н	М	-		-			_	-	-	17	(-1		•	•	• •	` '	• •	• •	• •	• •	• •		17									
ARG P	ARG P				ASP P				ASP P					LEU P											PHE P	PHE P			PHE P			ASP P		ASP P	ASP P	ASP P	ASP P	ASP P
CZ	NHT																					; ປີ	GB	ຶ່	CD	CE1	CZ	CE2	CD2	ບ	0	Z	G	8	ង	001	002	ບ
0	2900	2901	2902	2903	2904	2905	2000	o c	> C	2	2 5	1 5	1 5	1 5	<u>ا</u> ا	1 5		' "	ַ כַ	' 5	' '	1 0		~	~	~	~	~	2928	ö	ö	9	Ö	Ö	Ö	9	0	o.
· E	MOTA	MOTA	MOTA	ATOM ATOM	MOTA	MOF	E 0 E 6	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM.	ATOM MOTA	MOEK	E OF C	E OE 4	E 0 E 4	ATOR	E CE	ATOM	ALOFA	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	ATOM	MOTA	ATOM

Claims

- 1. A crystal structure of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex, characterised by the atomic co-ordinates of Annex 1.
- 2. A crystal structure as claimed in claim 1, wherein the interactions between $E2F_{(409-426)}$ and pRb comprise one or more of the following interactions:

E2F ₍₄₀₉₋₄₂₆₎ residue	pRb residue
Leu ₄₀₉	Lys ₅₄₈
Tyr ₄₁₁	Glu ₅₅₁
Tyr ₄₁₁	Ile ₅₃₂
Tyr ₄₁₁	Glu ₅₅₄
His ₄₁₂	Arg ₆₅₆
His ₄₁₂	Lys ₆₅₃
Gly ₄₁₄	Glu ₅₃₃
Gly ₄₁₄	Lys ₆₅₂
Leu ₄₁₅	Leu ₆₄₉
Leu ₄₁₅	Glu ₅₅₃
Leu ₄₁₅	Lys ₅₃₇
Glu ₄₁₇	Lys ₅₃₇
Gly ₄₁₈	Arg ₄₆₇
Glu ₄₁₉	Thr ₆₄₅
Arg ₄₂₂	Glu ₄₆₄
Asp ₄₂₃	Arg ₄₆₇
Leu ₄₂₄	Lys ₅₃₀
Phe ₄₂₅	Phe ₄₈₂
Phe ₄₂₅	Lys ₄₇₅

- 3. An assay to identify an agent which modulates the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎, the assay comprising:
- a) combining together pRb, E2F₍₄₀₉₋₄₂₆₎ and an agent, under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ form a complex;

- b) obtaining a crystal structure of any pRb/ E2F₍₄₀₉₋₄₂₆₎ complex; and
- c) analysing the crystal structure to determine whether the agent is an agent which modulates the interaction between pRb and E2F₍₄₀₉₋₄₂₆₎.
 - 4. An assay, as claimed in claim 3, wherein the combining of the components is pRb with the agent and then $E2F_{(409-426)}$.
- An assay as claimed in claim 3, wherein the combining of the components is E2F₍₄₀₉₋₄₂₆₎ with the agent and then pRb.
 - 6. An assay as claimed in claim 3, wherein the combining of the components is pRb with E2F₍₄₀₉₋₄₂₆₎ and then the agent.
 - 7. A method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising selecting an agent using the three-dimensional atomic coordinates of Annex 1.
- A method as claimed in claim 7, wherein said selection is performed in conjunction with computer modeling.
 - 9. A method as claimed in claim 7 or 8, wherein the method further comprises the steps of:

- a) contacting the selected agent with pRb and E2F₍₄₀₉₋₄₂₆₎ under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex; and
- b) measuring the binding affinity of pRb to E2F₍₄₀₉₋₄₂₆₎ in the presence of the agent and comparing the binding affinity to that of pRb to E2F₍₄₀₉₋₄₂₆₎ when in the absence of the agent, wherein an agent modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex when there is a change in the binding affinity of pRb to E2F₍₄₀₉₋₄₂₆₎ when in the presence of the agent.
- 10. A method as claimed in claim 9, wherein the method further comprising:

- a) growing a supplementary crystal from a solution containing pRb and E2F₍₄₀₉₋₄₂₆₎ and the selected agent where said agent changes the binding affinity of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex;
- b) determining the three-dimensional atomic coordinates of the supplementary crystal by X-ray diffraction using molecular replacement analysis;
 - c) comparing the three dimensional coordinates with those for the complex as claimed in claim 1; and
 - d) selecting a second generation agent using the three-dimensional atomic coordinates determined for the supplementary crystal.
 - 11. A method as claimed in claim 10, wherein said selection is performed in conjunction with computer modeling.
- 25 12. A method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:
 - a) contacting a selected agent with pRb and E2F₍₄₀₉₋₄₂₆₎ under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex; and

- b) measuring the binding affinity of pRb to E2F₍₄₀₉₋₄₂₆₎ in the presence of the agent and comparing the binding affinity to that of pRb to E2F₍₄₀₉₋₄₂₆₎ when in the absence of the agent, wherein an agent modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex when there is a change in the binding affinity of pRb to E2F₍₄₀₉₋₄₂₆₎ when in the presence of the agent.
- 13. A method as claimed in claim 12, wherein the method further comprising:
- a) growing a supplementary crystal from a solution containing pRb and E2F₍₄₀₉₋₄₂₆₎ and the selected agent where said agent changes the binding affinity of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex under conditions in which pRb and E2F₍₄₀₉₋₄₂₆₎ can form a complex;
 - b) determining the three-dimensional atomic coordinates of the supplementary crystal by X-ray diffraction using molecular replacement analysis;
 - c) comparing the three dimensional coordinates with those for the complex as claimed in claim 1; and
 - d) selecting a second generation agent using the three-dimensional atomic coordinates determined for the supplementary crystal.
- 14. A method as claimed in claim 13, wherein said selection is performed in conjunction with computer modeling.
 - 15. A method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:
 - a) selecting an agent;

10

15

- 25b) co-crystalising pRb with the agent;
 - c) determining the three dimensional coordinates of the pRb-agent association by X-ray diffraction using molecular replacement analysis; and
 - d) comparing the three dimensional coordinates with those of the complex as claimed in claim 1.

- 16. A method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:
- a) selecting an agent;
- b) crystalising pRb and soaking the agent into the crystal;
 - c) determining the three dimensional coordinates of the pRb-agent association by X-ray diffraction using molecular replacement analysis; and
 - d) comparing the three dimensional coordinates with those of the complex as claimed in claim 1.

17. A method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:

a) selecting an agent;

10

- b) co-crystalising pRb, E2F₍₄₀₉₋₄₂₆₎ and the agent;
- c) determining the three dimensional coordinates of the pRb-E2F-agent association by X-ray diffraction using molecular replacement analysis; and
 - d) comparing the three dimensional coordinates with those of the complex as claimed in claim 1.
- 20 18. A method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:
 - a) selecting an agent;
 - b) co-crystalising pRb and E2F₍₄₀₉₋₄₂₆₎ and soaking the agent into the crystal;
 - c) determining the three dimensional coordinates of the pRb-E2F-agent association by X-ray diffraction using molecular replacement analysis; and
 - d) comparing the three dimensional coordinates with those of the complex as claimed in claim 1.

- 19. A method as claimed in any one of claims 15 to 18, wherein the methods further comprises selecting a second generation agent using the three dimensional atomic coordinates determined.
- 5 20. A method as claimed in any one of claims 15 to 28, wherein the agent is selected using the three dimensional atomic coordinates of Annex 1.
 - 21. A method as claimed in claim 20, wherein the selection is performed in conjunction with computer modeling.
 - 22. A method of identifying an agent as claimed in any one of claims 7 to 21, wherein the selected agent and/or the second generation agent mimics a structural feature of E2F₍₄₀₉₋₄₂₆₎ when said E2F₍₄₀₉₋₄₂₆₎ is bound to pRb.
- 23. A method as claimed in claim 7 or 8, wherein method comprises the further steps of:
 - a) contacting the selected agent with the pRb/E2F₍₄₀₉₋₄₂₆₎ complex; and
 - b) determining whether the agent affects the stability of the complex.
- 20 24. A method as claimed in claim 23, wherein the determination is with fluorescence polarization.
 - 25. A method of identifying an agent that modulates a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, comprising:
- a) contacting a fluorescently tagged E2F₍₄₀₉₋₄₂₆₎ peptide (E2F-fluoroperptide) with pRb to allow pRb/E2F-fluoropeptide complex formation;
 - b) detecting the fluorescence polarization:
 - c) adding a selected agent; and

d) detecting the fluorescence polarization in the presence of the agent.

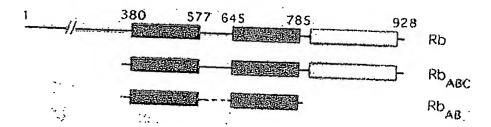
- 26. A method as claimed in claim 25, wherein an increase in fluorescence polarization in the presence of the agent indicates that the agent destabilises the complex.
- 27. A method as claimed in claim 25 or 26, wherein the method comprises the further step of adding untagged E2F₍₄₀₉₋₄₂₆₎ and detecting fluorescence polarization.
- 28. A method as claimed in claim 27, wherein if fluorescence polarization decreases, on addition of the untagged E2F₍₄₀₉₋₄₂₆₎, the agent does not stabilise the complex.

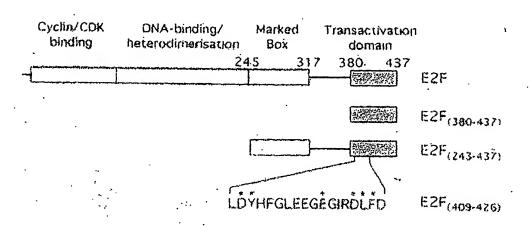
20

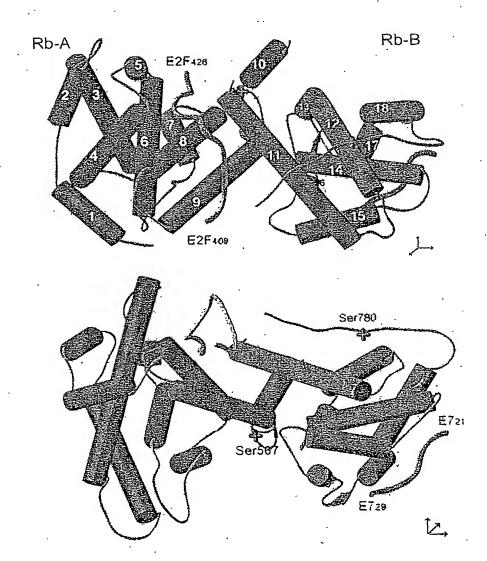
- 29. A method as claimed in claim 27 or 28, wherein if there is no substantial change in fluorescence polarization, on addition of the untagged E2F₍₄₀₉₋₄₂₆₎, the agent stabilises the complex.
 - 30. A method as claimed in any one of claims 9 to 14, wherein the binding affinity is measured by isothermal titration calorimetry.
 - 31. A method as claimed in any one of claims 9 to 14, wherein the binding affinity is measure by Surface Plasmon Resonance (SPR).
 - 32. An agent, that modulates the interaction between pRb and $E2F_{(409-426)}$, identified by a method as claimed in any one of claims 3 to 31.
 - 33. An agent, as claimed in claim 32, for use as an apoptosis promoting factor in the prevention or treatment of proliferative diseases.

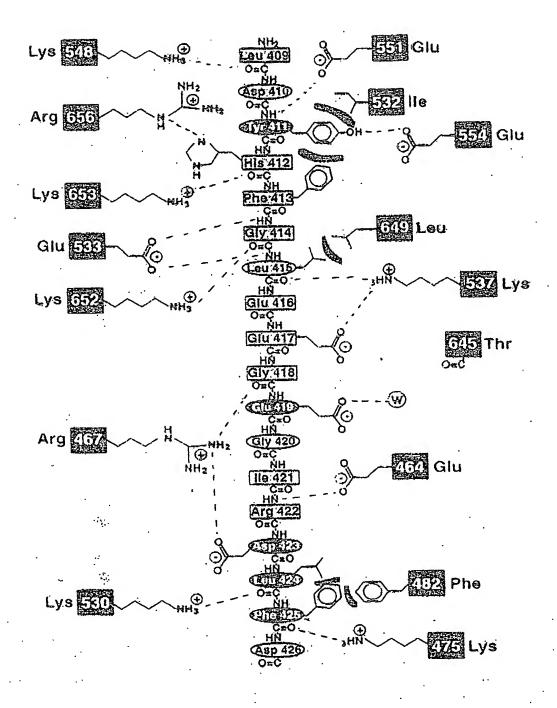
- 34. An agent as claimed in claim 32 or 33, wherein the agent is for use in preventing or treating cancer, which may be pancreatic cancer and related diseases.
- 35. The use of an agent, which modulates the formation of a pRb/E2F₍₄₀₉₋₄₂₆₎ complex, identified by a method as claimed in any one of claims 3 to 31, in the manufacture of a medicament for the prevention or treatment of proliferative diseases.
- 36. The use of an agent as claimed in claim 35, wherein the proliferative diseases are cancer, preferably pancreatic cancer and related diseases.

- 37. The use of the atomic co-ordinates of the crystal structure as claimed in claim 1 or 2, for identifying an agent that modulates the formation of a pRb/E2F₍₄₀₉₋₄₂₆₎ complex.
- 38. Computer readable media comprising a data storage material encoded with computer readable data, wherein said computer readable data comprises a set of atomic co-ordinates of the pRb/E2F₍₄₀₉₋₄₂₆₎ complex of Annex 1 recorded thereon.









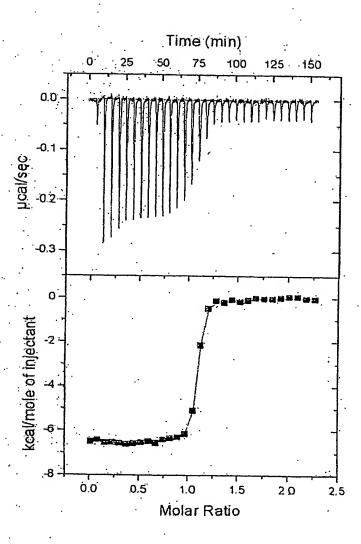


Figure 2B

Binding Constants (μM)	Rb _{AB}	Rb _{ABC}
E2F (409-426)	0.34 ± 0.02	0.3 ±0.03
E2F (380-437)	0.16 ±0.01	0.1 ±0.01
E2F (243-437)	<0.01	<0.01

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

☐ BLACK BORDERS
☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
☐ FADED TEXT OR DRAWING
☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
☐ SKEWED/SLANTED IMAGES
☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
☐ GRAY SCALE DOCUMENTS
LINES OR MARKS ON ORIGINAL DOCUMENT
☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

IMAGES ARE BEST AVAILABLE COPY.

☐ OTHER:

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.